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(57) Abstract  Novel polynucleotides and the proteins encoded thereby are disclosed.			

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## 5 SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

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FIELD OF THE INVENTION

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins.

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BACKGROUND OF THE INVENTION

Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques 25 clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader 30 sequence motif, as well as various PCR-based or low stringency hybridization cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity by virtue of their secreted nature in the case of leader sequence cloning, or by virtue of the cell or tissue source in the case of PCR-based techniques. It is to these proteins and the 35 polynucleotides encoding them that the present invention is directed.

SUMMARY OF THE INVENTION

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;
- 5 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 126 to nucleotide 485;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485;
- 10 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;
- 15 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;
- 20 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:2;
- 25 (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any 30 one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:1.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:1 from nucleotide 126 to nucleotide 485; the nucleotide sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485; the nucleotide sequence of the full-length protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804; or the 5 nucleotide sequence of a mature protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the 10 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:2, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising the amino acid sequence from amino acid 55 to amino acid 64 of SEQ 15 ID NO:2.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:1.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

20 (a) a process comprising the steps of:  
(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(aa) SEQ ID NO:1, but excluding the poly(A) tail at the  
25 3' end of SEQ ID NO:1; and  
(ab) the nucleotide sequence of the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;  
(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and  
30 (iii) isolating the DNA polynucleotides detected with the probe(s);  
and  
(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:1, but excluding the poly(A) tail at the 3' end of SEQ ID NO:1; and

(bb) the nucleotide sequence of the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

10 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:1, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:1 to

15 a nucleotide sequence corresponding to the 3' end of SEQ ID NO:1, but excluding the poly(A) tail at the 3' end of SEQ ID NO:1. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:1 from nucleotide 126 to nucleotide 485, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of

20 SEQ ID NO:1 from nucleotide 126 to nucleotide 485, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:1 from nucleotide 126 to nucleotide 485. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485, and extending contiguously from a

25 nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 30 consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2; and

(c) the amino acid sequence encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:2. In further preferred 5 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:2, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising the amino acid sequence from 10 amino acid 55 to amino acid 64 of SEQ ID NO:2.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3;

15 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3 from nucleotide 130 to nucleotide 2286;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3 from nucleotide 214 to nucleotide 2286;

20 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb3\_1 deposited under accession number ATCC 98804;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;

25 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb3\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;

30 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:4;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:4;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;

5 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:3.

10 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:3 from nucleotide 130 to nucleotide 2286; the nucleotide sequence of SEQ ID NO:3 from nucleotide 214 to nucleotide 2286; the nucleotide sequence of the full-length protein coding sequence of clone vb3\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb3\_1 deposited under 15 accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment 20 preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:4, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising the amino acid sequence from amino acid 354 to amino acid 363 of SEQ ID NO:4.

25 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:3.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

30 (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(aa) SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3; and

(ab) the nucleotide sequence of the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

5 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

10 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3; and

15 (bb) the nucleotide sequence of the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

20 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:3 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3. Also preferably the polynucleotide isolated  
25 according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3 from nucleotide 130 to nucleotide 2286, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:3 from nucleotide 130 to nucleotide 2286, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:3 from nucleotide 130 to  
30 nucleotide 2286. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3 from nucleotide 214 to nucleotide 2286, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:3 from

nucleotide 214 to nucleotide 2286, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:3 from nucleotide 214 to nucleotide 2286.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 5 consisting of:

- (a) the amino acid sequence of SEQ ID NO:4;
- (b) a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4; and
- (c) the amino acid sequence encoded by the cDNA insert of clone

10 vb3\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:4. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:4, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising the amino acid sequence from amino acid 354 to amino acid 363 of SEQ ID NO:4.

In one embodiment, the present invention provides a composition comprising an 20 isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:6;

5 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:6;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

10 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

15 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:5.

20 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522; the nucleotide sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522; the nucleotide sequence of the full-length protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the 25 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:6, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising the amino acid sequence from amino acid 53 to amino acid 62 of SEQ 30 ID NO:6.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:5.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:5, but excluding the poly(A) tail at the 3' end of SEQ ID NO:5; and
    - (ab) the nucleotide sequence of the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);

15 and

- (b) a process comprising the steps of:
  - (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (ba) SEQ ID NO:5, but excluding the poly(A) tail at the 3' end of SEQ ID NO:5; and
    - (bb) the nucleotide sequence of the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:5, and extending 30 contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:5 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:5, but excluding the poly(A) tail at the 3' end of SEQ ID NO:5. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522, and extending

contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522. Also preferably the polynucleotide isolated according to the above 5 process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522.

10 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:6;
- (b) a fragment of the amino acid sequence of SEQ ID NO:6, the 15 fragment comprising eight contiguous amino acids of SEQ ID NO:6; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:6. In further preferred 20 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:6, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising the amino acid sequence from 25 amino acid 53 to amino acid 62 of SEQ ID NO:6.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 176 to nucleotide 502;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804;

5 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804;

10 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:8;

15 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:8;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

20 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:7.

25 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502; the nucleotide sequence of SEQ ID NO:7 from nucleotide 176 to nucleotide 502; the nucleotide sequence of the full-length protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment

preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:8, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising the amino acid sequence from amino acid 59 to amino acid 68 of SEQ 5 ID NO:8.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:7.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- 10 (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:7, but excluding the poly(A) tail at the 15 3' end of SEQ ID NO:7; and
    - (ab) the nucleotide sequence of the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the 20 probe(s);
- and
- (b) a process comprising the steps of:
  - (i) preparing one or more polynucleotide primers that 25 hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (ba) SEQ ID NO:7, but excluding the poly(A) tail at the 3' end of SEQ ID NO:7; and
    - (bb) the nucleotide sequence of the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:7 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:7, but excluding the 5 poly(A) tail at the 3' end of SEQ ID NO:7. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502, to a nucleotide sequence 10 corresponding to the 3' end of said sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7 from nucleotide 176 to nucleotide 502, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:7 from 15 nucleotide 176 to nucleotide 502, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:7 from nucleotide 176 to nucleotide 502.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- 20 (a) the amino acid sequence of SEQ ID NO:8;
- (b) a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;
- 25 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:8. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids
- 30 of SEQ ID NO:8, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising the amino acid sequence from amino acid 59 to amino acid 68 of SEQ ID NO:8.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 128 to nucleotide 436;
- 5 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804;
- 10 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804;
- 15 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:10;
- 20 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:10;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- 25 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:9.

30 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:9 from nucleotide 128 to nucleotide 436; the nucleotide sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436; the nucleotide sequence of the full-length protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804; or the

nucleotide sequence of a mature protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the 5 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:10, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the 10 fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:10.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:9.

Further embodiments of the invention provide isolated polynucleotides produced 15 according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

20 (aa) SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9; and

(ab) the nucleotide sequence of the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;

25 (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

30 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9; and

(bb) the nucleotide sequence of the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

5 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:9 to 10 a nucleotide sequence corresponding to the 3' end of SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9 from nucleotide 128 to nucleotide 436, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of 15 SEQ ID NO:9 from nucleotide 128 to nucleotide 436, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:9 from nucleotide 128 to nucleotide 436. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436, and extending contiguously from a 20 nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 25 consisting of:

(a) the amino acid sequence of SEQ ID NO:10;

(b) a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10; and

(c) the amino acid sequence encoded by the cDNA insert of clone

30 vb6\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:10. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:10, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:10.

5 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:12;
- 25 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:12;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 30 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:11.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250; the nucleotide sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250; the nucleotide sequence of the full-length protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:12, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising the amino acid sequence from amino acid 180 to amino acid 189 of SEQ ID NO:12.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:11.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11; and
    - (ab) the nucleotide sequence of the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11; and

(bb) the nucleotide sequence of the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;

10 (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:11 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250.

30 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:12;

(b) a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12; and

(c) the amino acid sequence encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;

5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:12. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids

10 of SEQ ID NO:12, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising the amino acid sequence from amino acid 180 to amino acid 189 of SEQ ID NO:12.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 615 to nucleotide 869;

(c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb8\_1 deposited under accession number ATCC 98804;

20 (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

(e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb8\_1 deposited under accession number ATCC 98804;

25 (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:14;

30 (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:14;

- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above ;
- 5 (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:13.

10 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:13 from nucleotide 615 to nucleotide 869; the nucleotide sequence of the full-length protein coding sequence of clone vb8\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb8\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the 15 polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:14, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising the amino acid sequence from amino acid 37 to amino acid 46 of SEQ ID NO:14.

20 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:13.

25 Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize 30 in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:13, but excluding the poly(A) tail at the 3' end of SEQ ID NO:13; and

(ab) the nucleotide sequence of the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

5 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:13, but excluding the poly(A) tail at the 3' end of SEQ ID NO:13; and

(bb) the nucleotide sequence of the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

10 (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

20 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:13, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:13 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:13, but excluding the poly(A) tail at the 3' end of SEQ ID NO:13. Also preferably the

25 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:13 from nucleotide 615 to nucleotide 869, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:13 from nucleotide 615 to nucleotide 869, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:13 from nucleotide

30 615 to nucleotide 869.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:14;

(b) a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14; and

(c) the amino acid sequence encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:14. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids

10 of SEQ ID NO:14, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising the amino acid sequence from amino acid 37 to amino acid 46 of SEQ ID NO:14.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15 from nucleotide 148 to nucleotide 1470;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15 from nucleotide 193 to nucleotide 1470;

20 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

25 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

30 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:16;

- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:16;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of 5 (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 10 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:15.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:15 from nucleotide 148 to nucleotide 1470; the nucleotide sequence of SEQ ID NO:15 from nucleotide 193 to nucleotide 1470; the nucleotide sequence of the full-length protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb9\_1 20 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:16, or a polynucleotide encoding a protein comprising a 25 fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising the amino acid sequence from amino acid 215 to amino acid 224 of SEQ ID NO:16.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:15.

30 Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (aa) SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15; and

(ab) the nucleotide sequence of the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

10 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

15 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15; and

20 (bb) the nucleotide sequence of the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:15 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15. Also preferably the 30 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15 from nucleotide 148 to nucleotide 1470, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:15 from nucleotide 148 to nucleotide 1470, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:15 from nucleotide

148 to nucleotide 1470. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15 from nucleotide 193 to nucleotide 1470, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:15 from 5 nucleotide 193 to nucleotide 1470, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:15 from nucleotide 193 to nucleotide 1470.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10 (a) the amino acid sequence of SEQ ID NO:16;  
(b) a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16; and  
(c) the amino acid sequence encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

15 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:16. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:16, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising the amino acid sequence from amino acid 215 to amino acid 224 of SEQ ID NO:16.

20

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17;  
(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 414;  
(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 217 to nucleotide 414;  
30 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748;

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748;
- 5 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:18;
- 10 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:18;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 15 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 20 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:17.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 414; the nucleotide sequence of SEQ ID NO:17 from nucleotide 217 to nucleotide 414; the nucleotide sequence of the full-length protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the 25 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:18, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the 30

fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:18.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:17.

5 Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

10 (aa) SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17; and

(ab) the nucleotide sequence of the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;

15 (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

20 (b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

25 (ba) SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17; and

(bb) the nucleotide sequence of the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

30 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:17, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ

15 ID NO:17 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 5 414, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 414, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 414. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID 10 NO:17 from nucleotide 217 to nucleotide 414, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:17 from nucleotide 217 to nucleotide 414, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:17 from nucleotide 217 to nucleotide 414.

20 In other embodiments, the present invention provides a composition comprising 15 a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:18;
- (b) a fragment of the amino acid sequence of SEQ ID NO:18, the fragment comprising eight contiguous amino acids of SEQ ID NO:18; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;

25 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:18. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:18, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:18.

30 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 169 to nucleotide 840;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840;

5 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

10 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

15 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:20;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:20;

20 (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

25 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:19.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID

30 NO:19 from nucleotide 169 to nucleotide 840; the nucleotide sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840; the nucleotide sequence of the full-length protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide

encodes the full-length or a mature protein encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment 5 preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:20, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment comprising the amino acid sequence from amino acid 107 to amino acid 116 of SEQ ID NO:20.

10 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:19.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

15 (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(aa) SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19; and

20 (ab) the nucleotide sequence of the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the 25 probe(s);

and

(b) a process comprising the steps of:

30 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19; and

(bb) the nucleotide sequence of the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

5 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:19 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19. Also preferably the

10 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19 from nucleotide 169 to nucleotide 840, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:19 from nucleotide 169 to nucleotide 840, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:19 from nucleotide 169 to nucleotide 840. Also preferably the polynucleotide isolated according to the above

15 process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840, to a nucleotide sequence corresponding to the 3' end of

20 said sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:20;

25 (b) a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins. Preferably such

30 protein comprises the amino acid sequence of SEQ ID NO:20. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:20, or a protein comprising a fragment of the amino acid sequence of SEQ

ID NO:20 having biological activity, the fragment comprising the amino acid sequence from amino acid 107 to amino acid 116 of SEQ ID NO:20.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- 5 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21;
- 10 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951;
- 15 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748;
- 20 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748;
- 25 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:22;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:22;
- 30 (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:21.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951; the nucleotide sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951; the nucleotide sequence of the full-length protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748; or the 5 nucleotide sequence of a mature protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the 10 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:22, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising the amino acid sequence from amino acid 69 to amino acid 78 of SEQ 15 ID NO:22.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:21.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

20 (a) a process comprising the steps of:  
(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(aa) SEQ ID NO:21, but excluding the poly(A) tail at the  
25 3' end of SEQ ID NO:21; and  
(ab) the nucleotide sequence of the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;  
(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and  
30 (iii) isolating the DNA polynucleotides detected with the probe(s);  
and  
(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:21, but excluding the poly(A) tail at the 3' end of SEQ ID NO:21; and

(bb) the nucleotide sequence of the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

10 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ 15 ID NO:21 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:21, but excluding the poly(A) tail at the 3' end of SEQ ID NO:21. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951, and extending contiguously from a nucleotide sequence corresponding to the 5' end 20 of said sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951, and extending contiguously from a 25 nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 30 consisting of:

(a) the amino acid sequence of SEQ ID NO:22;

(b) a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:22. In further preferred 5 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:22, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising the amino acid sequence 10 from amino acid 69 to amino acid 78 of SEQ ID NO:22.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23;
- 15 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide 493;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc7\_1 deposited under accession number ATCC 98748;
- 20 (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc7\_1 deposited under accession number ATCC 98748;
- 25 (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:24;
- 30 (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:24;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;

- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above ;
- (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and
- 5 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:23.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide 493; the nucleotide sequence of the full-length 10 protein coding sequence of clone vc7\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc7\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748. In further preferred 15 embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:24, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having 20 biological activity, the fragment comprising the amino acid sequence from amino acid 56 to amino acid 65 of SEQ ID NO:24.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:23.

Further embodiments of the invention provide isolated polynucleotides produced 25 according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - 30 (aa) SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23; and
    - (ab) the nucleotide sequence of the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;

- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

5 and

- (b) a process comprising the steps of:
  - (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (ba) SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23; and
    - (bb) the nucleotide sequence of the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:23, and

20 extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:23 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide

25 493, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide 493, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide 493.

In other embodiments, the present invention provides a composition comprising

30 a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:24;
- (b) a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;  
the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:24. In further preferred 5 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:24, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising the amino acid sequence 10 from amino acid 56 to amino acid 65 of SEQ ID NO:24.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25 from nucleotide 33 to nucleotide 407;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25 from nucleotide 99 to nucleotide 407;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc9\_1 deposited under accession number ATCC 98748;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc9\_1 deposited under accession number ATCC 98748;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:26;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:26;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- 5 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:25.

10 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:25 from nucleotide 33 to nucleotide 407; the nucleotide sequence of SEQ ID NO:25 from nucleotide 99 to nucleotide 407; the nucleotide sequence of the full-length protein coding sequence of clone vc9\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc9\_1 deposited under 15 accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment 20 preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:26, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising the amino acid sequence from amino acid 57 to amino acid 66 of SEQ ID NO:26.

25 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:25.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25; and

(ab) the nucleotide sequence of the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

5 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

10 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25; and

15 (bb) the nucleotide sequence of the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

20 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:25, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:25 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25. Also preferably the

25 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:25 from nucleotide 33 to nucleotide 407, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:25 from nucleotide 33 to nucleotide 407, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:25 from nucleotide

30 33 to nucleotide 407. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:25 from nucleotide 99 to nucleotide 407, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:25 from

nucleotide 99 to nucleotide 407, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:25 from nucleotide 99 to nucleotide 407.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 5 consisting of:

- (a) the amino acid sequence of SEQ ID NO:26;
- (b) a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26; and
- (c) the amino acid sequence encoded by the cDNA insert of clone 10 vc9\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:26. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment preferably 15 comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:26, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising the amino acid sequence from amino acid 57 to amino acid 66 of SEQ ID NO:26.

In one embodiment, the present invention provides a composition comprising an 20 isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871;
- (c) a polynucleotide comprising the nucleotide sequence of the full- 25 length protein coding sequence of clone vc10\_1 deposited under accession number ATCC 98748;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;
- (e) a polynucleotide comprising the nucleotide sequence of a mature 30 protein coding sequence of clone vc10\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:28;

5 (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:28;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above ;

10 (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:27.

15 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871; the nucleotide sequence of the full-length protein coding sequence of clone vc10\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc10\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the 20 polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably comprising eight (more preferably twenty, most 25 preferably thirty) contiguous amino acids of SEQ ID NO:28, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising the amino acid sequence from amino acid 111 to amino acid 120 of SEQ ID NO:28.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 30 ID NO:27.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (aa) SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27; and

(ab) the nucleotide sequence of the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

10 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

15 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27; and

20 (bb) the nucleotide sequence of the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:27, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:27 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27. Also preferably the 30 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871, to a nucleotide

sequence corresponding to the 3' end of said sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 5 consisting of:

- (a) the amino acid sequence of SEQ ID NO:28;
- (b) a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28; and
- (c) the amino acid sequence encoded by the cDNA insert of clone 10 vc10\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:28. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably 15 comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:28, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising the amino acid sequence from amino acid 111 to amino acid 120 of SEQ ID NO:28.

In one embodiment, the present invention provides a composition comprising an 20 isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide 657;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc11\_1 deposited under accession number 25 ATCC 98748;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc11\_1 deposited under accession number ATCC 98748;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:30;

5 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:30;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

10 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 15 25% of the length of SEQ ID NO:29.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide 657; the nucleotide sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657; the nucleotide sequence of the full-length protein 20 coding sequence of clone vc11\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc11\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the 25 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:30, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the 30 fragment comprising the amino acid sequence from amino acid 78 to amino acid 87 of SEQ ID NO:30.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:29.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(aa) SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29; and

(ab) the nucleotide sequence of the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

15 and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29; and

(bb) the nucleotide sequence of the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:29, and 30 extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:29 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide

657, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide 657, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide 657. Also preferably the polynucleotide isolated according to the above 5 process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657.

10 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:30;
- (b) a fragment of the amino acid sequence of SEQ ID NO:30, the 15 fragment comprising eight contiguous amino acids of SEQ ID NO:30; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:30. In further preferred 20 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:30, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment comprising the amino acid sequence 25 from amino acid 78 to amino acid 87 of SEQ ID NO:30.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:31;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID 30 NO:31 from nucleotide 228 to nucleotide 662;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:31 from nucleotide 327 to nucleotide 662;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc14\_1 deposited under accession number ATCC 98748;

5 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc14\_1 deposited under accession number ATCC 98748;

10 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:32;

15 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:32;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;

20 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:31.

25 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:31 from nucleotide 228 to nucleotide 662; the nucleotide sequence of SEQ ID NO:31 from nucleotide 327 to nucleotide 662; the nucleotide sequence of the full-length protein coding sequence of clone vc14\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vc14\_1 deposited under 30 accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment

preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:32, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising the amino acid sequence from amino acid 67 to amino acid 76 of SEQ 5 ID NO:32.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:31.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

10

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

15

(aa) SEQ ID NO:31, but excluding the poly(A) tail at the 3' end of SEQ ID NO:31; and

(ab) the nucleotide sequence of the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;

20

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

25

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

30

(ba) SEQ ID NO:31, but excluding the poly(A) tail at the 3' end of SEQ ID NO:31; and

(bb) the nucleotide sequence of the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:31, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:31 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:31, but 5 excluding the poly(A) tail at the 3' end of SEQ ID NO:31. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:31 from nucleotide 228 to nucleotide 662, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:31 from nucleotide 228 to nucleotide 662, to a nucleotide 10 sequence corresponding to the 3' end of said sequence of SEQ ID NO:31 from nucleotide 228 to nucleotide 662. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:31 from nucleotide 327 to nucleotide 662, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:31 from 15 nucleotide 327 to nucleotide 662, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:31 from nucleotide 327 to nucleotide 662.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- 20 (a) the amino acid sequence of SEQ ID NO:32;
- (b) a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;
- 25 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:32. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids
- 30 of SEQ ID NO:32, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising the amino acid sequence from amino acid 67 to amino acid 76 of SEQ ID NO:32.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667;

5 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784;

10 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784;

15 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:34;

20 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:34;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

25 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 30 25% of the length of SEQ ID NO:33.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667; the nucleotide sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667; the nucleotide sequence of the full-length protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784; or the

nucleotide sequence of a mature protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the 5 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:34, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the 10 fragment comprising the amino acid sequence from amino acid 89 to amino acid 98 of SEQ ID NO:34.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:33.

Further embodiments of the invention provide isolated polynucleotides produced 15 according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

20 (aa) SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33; and

(ab) the nucleotide sequence of the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;

25 (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

30 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33; and

(bb) the nucleotide sequence of the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

5 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:33, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ 10 ID NO:33 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667, and extending contiguously from a nucleotide sequence corresponding to the 5' end 15 of said sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667, to a nucleotide sequence corresponding to the 3' end of 20 said sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667. 25

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:34;

(b) a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34; and

(c) the amino acid sequence encoded by the cDNA insert of clone

30 vc16\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:34. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:34, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising the amino acid sequence from amino acid 89 to amino acid 98 of SEQ ID NO:34.

5 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 8 to nucleotide 355;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc17\_1 deposited under accession number 15 ATCC 98784;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc17\_1 deposited under accession number ATCC 20 98784;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:36;
- 25 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:36;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:35.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID 5 NO:35 from nucleotide 8 to nucleotide 355; the nucleotide sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355; the nucleotide sequence of the full-length protein coding sequence of clone vc17\_1 deposited under accession number ATCC 98784; or the nucleotide sequence of a mature protein coding sequence of clone vc17\_1 deposited under accession number ATCC 98784. In other preferred embodiments, the polynucleotide 10 encodes the full-length or a mature protein encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous 15 amino acids of SEQ ID NO:36, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising the amino acid sequence from amino acid 53 to amino acid 62 of SEQ ID NO:36.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:35.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize 25 in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(aa) SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35; and

(ab) the nucleotide sequence of the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35; and

(bb) the nucleotide sequence of the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;

10 (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:35 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35 from nucleotide 8 to nucleotide 355, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:35 from nucleotide 8 to nucleotide 355, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:35 from nucleotide 8 to nucleotide 355. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355.

20 30 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:36;

(b) a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;

5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:36. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids

10 of SEQ ID NO:36, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising the amino acid sequence from amino acid 53 to amino acid 62 of SEQ ID NO:36.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37 from nucleotide 1031 to nucleotide 1252;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37 from nucleotide 1100 to nucleotide 1252;

20 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785;

25 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:38;

- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:38;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of 5 (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 10 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:37.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:37 from nucleotide 1031 to nucleotide 1252; the nucleotide sequence of SEQ ID NO:37 from nucleotide 1100 to nucleotide 1252; the nucleotide sequence of the full-length protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785; or the nucleotide sequence of a mature protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785. In yet other preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:38 from amino acid 29 to amino acid 74. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:38, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising the amino acid sequence from amino acid 32 to amino acid 41 of SEQ ID NO:38.

30 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:37.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (aa) SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37; and

(ab) the nucleotide sequence of the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

10 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

15 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37; and

20 (bb) the nucleotide sequence of the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:37 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37. Also preferably the 30 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37 from nucleotide 1031 to nucleotide 1252, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:37 from nucleotide 1031 to nucleotide 1252, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:37 from nucleotide

1031 to nucleotide 1252. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37 from nucleotide 1100 to nucleotide 1252, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:37 from 5 nucleotide 1100 to nucleotide 1252, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:37 from nucleotide 1100 to nucleotide 1252.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10 (a) the amino acid sequence of SEQ ID NO:38;  
(b) the amino acid sequence of SEQ ID NO:38 from amino acid 29 to amino acid 74;  
(c) a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38; and  
15 (d) the amino acid sequence encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:38 or the amino acid sequence of SEQ ID NO:38 from amino acid 29 to amino acid 74. In further preferred embodiments, 20 the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:38, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising the amino acid sequence from amino 25 acid 32 to amino acid 41 of SEQ ID NO:38.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

30 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39;  
(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482;  
(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39 from nucleotide 214 to nucleotide 1482;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc23\_1 deposited under accession number ATCC 98784;

5 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc23\_1 deposited under accession number ATCC 98784;

10 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:40;

15 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:40;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

20 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:39.

25 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482; the nucleotide sequence of SEQ ID NO:39 from nucleotide 214 to nucleotide 1482; the nucleotide sequence of the full-length protein coding sequence of clone vc23\_1 deposited under accession number ATCC 98784; or the nucleotide sequence of a mature protein coding sequence of clone vc23\_1 deposited under 30 accession number ATCC 98784. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment

preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:40, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising the amino acid sequence from amino acid 226 to amino acid 235 of 5 SEQ ID NO:40.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:39.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

10 (a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

15 (aa) SEQ ID NO:39, but excluding the poly(A) tail at the 3' end of SEQ ID NO:39; and

(ab) the nucleotide sequence of the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

20 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

25 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

30 (ba) SEQ ID NO:39, but excluding the poly(A) tail at the 3' end of SEQ ID NO:39; and

(bb) the nucleotide sequence of the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:39, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:39 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:39, but 5 excluding the poly(A) tail at the 3' end of SEQ ID NO:39. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482, to a nucleotide 10 sequence corresponding to the 3' end of said sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:39 from nucleotide 214 to nucleotide 1482, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:39 from 15 nucleotide 214 to nucleotide 1482, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:39 from nucleotide 214 to nucleotide 1482.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- 20 (a) the amino acid sequence of SEQ ID NO:40;
- (b) a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;
- 25 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:40. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids
- 30 of SEQ ID NO:40, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising the amino acid sequence from amino acid 226 to amino acid 235 of SEQ ID NO:40.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413;

5 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784;

10 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784;

15 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:42;

20 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:42;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

25 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 30 25% of the length of SEQ ID NO:41.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413; the nucleotide sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413; the nucleotide sequence of the full-length protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784; or the

nucleotide sequence of a mature protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the 5 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:42, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the 10 fragment comprising the amino acid sequence from amino acid 38 to amino acid 47 of SEQ ID NO:42.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:41.

Further embodiments of the invention provide isolated polynucleotides produced 15 according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

20 (aa) SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41; and

(ab) the nucleotide sequence of the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;

25 (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

30 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41; and

(bb) the nucleotide sequence of the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

5 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ 10 ID NO:41 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413, and extending contiguously from a nucleotide sequence corresponding to the 5' end 15 of said sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413, to a nucleotide sequence corresponding to the 3' end of 20 said sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 25 consisting of:

(a) the amino acid sequence of SEQ ID NO:42;

(b) a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42; and

(c) the amino acid sequence encoded by the cDNA insert of clone 30 vc25\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:42. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:42, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment comprising the amino acid sequence from amino acid 38 to amino acid 47 of SEQ ID NO:42.

5 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 87 to nucleotide 1409;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:44;
- 25 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:44;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 30 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:43.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID 5 NO:43 from nucleotide 87 to nucleotide 1409; the nucleotide sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409; the nucleotide sequence of the full-length protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784; or the nucleotide sequence of a mature protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784. In other preferred embodiments, the polynucleotide 10 encodes the full-length or a mature protein encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous 15 amino acids of SEQ ID NO:44, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising the amino acid sequence from amino acid 215 to amino acid 224 of SEQ ID NO:44.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:43.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:  
(i) preparing one or more polynucleotide probes that hybridize 25 in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(aa) SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43; and  
(ab) the nucleotide sequence of the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;  
(ii) hybridizing said probe(s) to human genomic DNA in 30 conditions at least as stringent as 4X SSC at 50 degrees C; and  
(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43; and

(bb) the nucleotide sequence of the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;

10 (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:43 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43 from nucleotide 87 to nucleotide 1409, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:43 from nucleotide 87 to nucleotide 1409, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:43 from nucleotide 87 to nucleotide 1409. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409.

20 25

30 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:44;

(b) a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;

5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:44. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids

10 of SEQ ID NO:44, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising the amino acid sequence from amino acid 215 to amino acid 224 of SEQ ID NO:44.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428;

20 (d) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 356 to nucleotide 1773;

(e) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804;

25 (f) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804;

30 (h) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

(i) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:46;

- (j) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:46;
- (k) a polynucleotide which is an allelic variant of a polynucleotide of 5 (a)-(h) above;
- (l) a polynucleotide which encodes a species homologue of the protein of (i) or (j) above ;
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j); and
- 10 (n) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j) and that has a length that is at least 25% of the length of SEQ ID NO:45.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428; the nucleotide sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428; the nucleotide sequence of SEQ ID NO:45 from nucleotide 356 to nucleotide 1773; the nucleotide sequence of the full-length protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide 15 encodes the full-length or a mature protein encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804. In yet other preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:46 from amino acid 1 to amino acid 97. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein 20 comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:46, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising the amino acid sequence from amino acid 56 25 to amino acid 65 of SEQ ID NO:46.

30 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:45.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (aa) SEQ ID NO:45, but excluding the poly(A) tail at the 3' end of SEQ ID NO:45; and

(ab) the nucleotide sequence of the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in

10 conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

15 (ba) SEQ ID NO:45, but excluding the poly(A) tail at the 3' end of SEQ ID NO:45; and

(bb) the nucleotide sequence of the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in

20 conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

25 (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:45 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:45, but excluding the poly(A) tail at the 3' end of SEQ ID NO:45. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428, to a nucleotide

sequence corresponding to the 3' end of said sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428, and extending contiguously from a 5 nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45 from nucleotide 356 to 10 nucleotide 1773, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:45 from nucleotide 356 to nucleotide 1773, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:45 from nucleotide 356 to nucleotide 1773.

In other embodiments, the present invention provides a composition comprising 15 a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:46;
- (b) the amino acid sequence of SEQ ID NO:46 from amino acid 1 to amino acid 97;
- 20 (c) a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such 25 protein comprises the amino acid sequence of SEQ ID NO:46 or the amino acid sequence of SEQ ID NO:46 from amino acid 1 to amino acid 97. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID 30 NO:46, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising the amino acid sequence from amino acid 56 to amino acid 65 of SEQ ID NO:46.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799;
- 5 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748;
- 10 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748;
- 15 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:48;
- 20 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:48;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 25 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 30 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:47.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799; the nucleotide sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799; the nucleotide sequence of the full-length protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748; or the

nucleotide sequence of a mature protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the 5 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:48, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the 10 fragment comprising the amino acid sequence from amino acid 290 to amino acid 299 of SEQ ID NO:48.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:47.

Further embodiments of the invention provide isolated polynucleotides produced 15 according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:47, but excluding the poly(A) tail at the 20 3' end of SEQ ID NO:47; and
    - (ab) the nucleotide sequence of the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;
  - (ii) hybridizing said probe(s) to human genomic DNA in 25 conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- and
- (b) a process comprising the steps of:
  - (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (ba) SEQ ID NO:47, but excluding the poly(A) tail at the 30 3' end of SEQ ID NO:47; and

(bb) the nucleotide sequence of the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

5 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:47, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ 10 ID NO:47 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:47, but excluding the poly(A) tail at the 3' end of SEQ ID NO:47. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799, and extending contiguously from a nucleotide sequence corresponding to the 5' end 15 of said sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799, to a nucleotide sequence corresponding to the 3' end of 20 said sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 25 consisting of:

(a) the amino acid sequence of SEQ ID NO:48;

(b) a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48; and

(c) the amino acid sequence encoded by the cDNA insert of clone 30 vd1\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:48. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:48, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising the amino acid sequence from amino acid 290 to amino acid 299 of SEQ ID NO:48.

5 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49;
- 10 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443;
- 15 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;
- 20 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:50;
- 25 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:50;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 30 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:49.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443; the nucleotide sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443; the nucleotide sequence of the full-length protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748; or the nucleotide sequence of a mature protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:50, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising the amino acid sequence from amino acid 57 to amino acid 66 of SEQ ID NO:50.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:49.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49; and

(bb) the nucleotide sequence of the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;

10 (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:49 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443.

30 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:50;

(b) a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50; and

(c) the amino acid sequence encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;

5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:50. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids

10 of SEQ ID NO:50, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising the amino acid sequence from amino acid 57 to amino acid 66 of SEQ ID NO:50.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51 from nucleotide 176 to nucleotide 1249;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51 from nucleotide 227 to nucleotide 1249;

20 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;

25 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;

30 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:52;

- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:52;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of 5 (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 10 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:51.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:51 from nucleotide 176 to nucleotide 1249; the nucleotide sequence of SEQ ID NO:51 from nucleotide 227 to nucleotide 1249; the nucleotide sequence of the full-length protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vd3\_1 20 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:52, or a polynucleotide encoding a protein comprising a 25 fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising the amino acid sequence from amino acid 174 to amino acid 183 of SEQ ID NO:52.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:51.

30 Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (aa) SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51; and

(ab) the nucleotide sequence of the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

10 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

15 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51; and

20 (bb) the nucleotide sequence of the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:51 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51. Also preferably the 30 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51 from nucleotide 176 to nucleotide 1249, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:51 from nucleotide 176 to nucleotide 1249, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:51 from nucleotide

176 to nucleotide 1249. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51 from nucleotide 227 to nucleotide 1249, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:51 from 5 nucleotide 227 to nucleotide 1249, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:51 from nucleotide 227 to nucleotide 1249.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10 (a) the amino acid sequence of SEQ ID NO:52;  
(b) a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52; and  
(c) the amino acid sequence encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;

15 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:52. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids  
20 of SEQ ID NO:52, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising the amino acid sequence from amino acid 174 to amino acid 183 of SEQ ID NO:52.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53;  
(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 1530;  
(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53 from nucleotide 145 to nucleotide 1530;  
30 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804;

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804;
- 5 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:54;
- 10 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:54;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- 15 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 20 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:53.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 1530; the nucleotide sequence of SEQ ID NO:53 from nucleotide 145 to nucleotide 1530; the nucleotide sequence of the full-length protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:54, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the

fragment comprising the amino acid sequence from amino acid 234 to amino acid 243 of SEQ ID NO:54.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:53.

5 Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

10

(aa) SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53; and

(ab) the nucleotide sequence of the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;

15

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

20

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

25

(ba) SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53; and

(bb) the nucleotide sequence of the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

30

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:53, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ

1530 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 5 1530, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 1530, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 1530. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID 10 NO:53 from nucleotide 145 to nucleotide 1530, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:53 from nucleotide 145 to nucleotide 1530, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:53 from nucleotide 145 to nucleotide 1530.

In other embodiments, the present invention provides a composition comprising 15 a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:54;
- (b) a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54; and
- (c) the amino acid sequence encoded by the cDNA insert of clone 20 vd4\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:54. In further preferred embodiments, the present invention provides a protein comprising a fragment of the 25 amino acid sequence of SEQ ID NO:54 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:54, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment comprising the amino acid sequence from amino acid 234 to amino acid 243 of SEQ ID NO:54.

30 In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1300;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300;

5 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;

10 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;

15 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:56;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:56;

20 (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

(l) a polynucleotide that hybridizes under stringent conditions to any 25 one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:55.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID 30 NO:55 from nucleotide 71 to nucleotide 1300; the nucleotide sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300; the nucleotide sequence of the full-length protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784; or the nucleotide sequence of a mature protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784. In other preferred embodiments, the polynucleotide

encodes the full-length or a mature protein encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment 5 preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:56, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising the amino acid sequence from amino acid 200 to amino acid 209 of SEQ ID NO:56.

10 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:55.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:55, but excluding the poly(A) tail at the 3' end of SEQ ID NO:55; and
    - (ab) the nucleotide sequence of the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);

25 and

- (b) a process comprising the steps of:
  - (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (ba) SEQ ID NO:55, but excluding the poly(A) tail at the 3' end of SEQ ID NO:55; and
    - (bb) the nucleotide sequence of the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

5 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:55, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:55 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:55, but excluding the poly(A) tail at the 3' end of SEQ ID NO:55. Also preferably the

10 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1300, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1300, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:55 from nucleotide

15 71 to nucleotide 1300. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300, to a nucleotide sequence corresponding to the 3' end

20 of said sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:56;

25 (b) a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56; and

(c) the amino acid sequence encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins. Preferably such

30 protein comprises the amino acid sequence of SEQ ID NO:56. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:56, or a protein comprising a fragment of the amino acid sequence of SEQ

ID NO:56 having biological activity, the fragment comprising the amino acid sequence from amino acid 200 to amino acid 209 of SEQ ID NO:56.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785;

10 (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804;

15 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804;

20 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:58;

25 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:58;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

30 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:57.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785; the nucleotide sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785; the nucleotide sequence of the full-length protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804; or the 5 nucleotide sequence of a mature protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the 10 present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:58, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising the amino acid sequence from amino acid 116 to amino acid 125 of 15 SEQ ID NO:58.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:57.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

20 (a) a process comprising the steps of:  
(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(aa) SEQ ID NO:57, but excluding the poly(A) tail at the  
25 3' end of SEQ ID NO:57; and  
(ab) the nucleotide sequence of the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;  
(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and  
30 (iii) isolating the DNA polynucleotides detected with the probe(s);  
and  
(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5 (ba) SEQ ID NO:57, but excluding the poly(A) tail at the 3' end of SEQ ID NO:57; and

(bb) the nucleotide sequence of the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

10 (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ 15 ID NO:57 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:57, but excluding the poly(A) tail at the 3' end of SEQ ID NO:57. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785, and extending contiguously from a nucleotide sequence corresponding to the 5' end 20 of said sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785, and extending contiguously from a 25 nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 30 consisting of:

(a) the amino acid sequence of SEQ ID NO:58;

(b) a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58; and

(c) the amino acid sequence encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:58. In further preferred 5 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:58, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising the amino acid sequence 10 from amino acid 116 to amino acid 125 of SEQ ID NO:58.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59;

15 (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59 from nucleotide 64 to nucleotide 1002;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59 from nucleotide 139 to nucleotide 1002;

20 (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vf1\_1 deposited under accession number ATCC 98784;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;

25 (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vf1\_1 deposited under accession number ATCC 98784;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;

30 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:60;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:60;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- 5 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:59.

10 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:59 from nucleotide 64 to nucleotide 1002; the nucleotide sequence of SEQ ID NO:59 from nucleotide 139 to nucleotide 1002; the nucleotide sequence of the full-length protein coding sequence of clone vf1\_1 deposited under accession number ATCC 98784; or the nucleotide sequence of a mature protein coding sequence of clone vf1\_1 deposited under 15 accession number ATCC 98784. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment 20 preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:60, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising the amino acid sequence from amino acid 151 to amino acid 160 of SEQ ID NO:60.

25 Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:59.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
  - 30 (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
    - (aa) SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59; and

(ab) the nucleotide sequence of the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

5 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

10 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59; and

15 (bb) the nucleotide sequence of the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

20 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:59 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59. Also preferably the 25 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59 from nucleotide 64 to nucleotide 1002, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:59 from nucleotide 64 to nucleotide 1002, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:59 from nucleotide 30 64 to nucleotide 1002. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59 from nucleotide 139 to nucleotide 1002, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:59 from

nucleotide 139 to nucleotide 1002, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:59 from nucleotide 139 to nucleotide 1002.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group 5 consisting of:

- (a) the amino acid sequence of SEQ ID NO:60;
- (b) a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf1\_1

10 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:60. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment preferably 15 comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:60, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising the amino acid sequence from amino acid 151 to amino acid 160 of SEQ ID NO:60.

In one embodiment, the present invention provides a composition comprising an 20 isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide 995;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804;

(g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:62;

5 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:62;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

10 (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

15 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:61.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide 995; the nucleotide sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995; the nucleotide sequence of the full-length protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:62, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising the amino acid sequence from amino acid 63 to amino acid 72 of SEQ ID NO:62.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:61.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(aa) SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61; and

(ab) the nucleotide sequence of the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

15 and

(b) a process comprising the steps of:

(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61; and

(bb) the nucleotide sequence of the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;

(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

(iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61, and 30 extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:61 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide

995, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide 995, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide 995. Also preferably the polynucleotide isolated according to the above 5 process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995.

10 In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:62;
- (b) a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;

15 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:62. In further preferred 20 embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:62, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising the amino acid sequence 25 from amino acid 63 to amino acid 72 of SEQ ID NO:62.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63 from nucleotide 104 to nucleotide 1369;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vi1\_1 deposited under accession number ATCC 98804;

5 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vi1\_1 deposited under accession number ATCC 98804;

10 (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:64;

15 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:64;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;

20 (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:63.

25 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369; the nucleotide sequence of SEQ ID NO:63 from nucleotide 104 to nucleotide 1369; the nucleotide sequence of the full-length protein coding sequence of clone vi1\_1 deposited under accession number ATCC 98804; or the nucleotide sequence of a mature protein coding sequence of clone vi1\_1 deposited under 30 accession number ATCC 98804. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment

preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:64, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising the amino acid sequence from amino acid 218 to amino acid 227 of 5 SEQ ID NO:64.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:63.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

10 (a) a process comprising the steps of:  
(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(aa) SEQ ID NO:63, but excluding the poly(A) tail at the  
15 3' end of SEQ ID NO:63; and  
(ab) the nucleotide sequence of the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;  
(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and  
20 (iii) isolating the DNA polynucleotides detected with the probe(s);

and

25 (b) a process comprising the steps of:  
(i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:  
(ba) SEQ ID NO:63, but excluding the poly(A) tail at the  
3' end of SEQ ID NO:63; and  
(bb) the nucleotide sequence of the cDNA insert of clone  
30 vi1\_1 deposited under accession number ATCC 98804;  
(ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;  
(iii) amplifying human DNA sequences; and  
(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:63, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:63 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:63, but 5 excluding the poly(A) tail at the 3' end of SEQ ID NO:63. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369, to a nucleotide 10 sequence corresponding to the 3' end of said sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:63 from nucleotide 104 to nucleotide 1369, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:63 from 15 nucleotide 104 to nucleotide 1369, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:63 from nucleotide 104 to nucleotide 1369.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- 20 (a) the amino acid sequence of SEQ ID NO:64;
- (b) a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;
- 25 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:64. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids
- 30 of SEQ ID NO:64, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising the amino acid sequence from amino acid 218 to amino acid 227 of SEQ ID NO:64.

In certain preferred embodiments, the polynucleotide is operably linked to an expression control sequence. The invention also provides a host cell, including bacterial,

yeast, insect and mammalian cells, transformed with such polynucleotide compositions. Also provided by the present invention are organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein.

5 Processes are also provided for producing a protein, which comprise:

- (a) growing a culture of the host cell transformed with such polynucleotide compositions in a suitable culture medium; and
- (b) purifying the protein from the culture.

The protein produced according to such methods is also provided by the present 10 invention.

Protein compositions of the present invention may further comprise a pharmaceutically acceptable carrier. Compositions comprising an antibody which specifically reacts with such protein are also provided by the present invention.

Methods are also provided for preventing, treating or ameliorating a medical 15 condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition comprising a protein of the present invention and a pharmaceutically acceptable carrier.

#### BRIEF DESCRIPTION OF THE DRAWINGS

20 Figures 1A and 1B are schematic representations of the pED6 and pNOTs vectors, respectively, used for deposit of clones disclosed herein.

#### DETAILED DESCRIPTION

##### ISOLATED PROTEINS AND POLYNUCLEOTIDES

25 Nucleotide and amino acid sequences, as presently determined, are reported below for each clone and protein disclosed in the present application. The nucleotide sequence of each clone can readily be determined by sequencing of the deposited clone in accordance with known methods. The predicted amino acid sequence (both full-length and mature forms) can then be determined from such nucleotide sequence. The amino 30 acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein and determining its sequence. For each disclosed protein applicants have identified what they have determined to be the reading frame best identifiable with sequence information available at the time of filing.

As used herein a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g., receptors) from the cell 5 in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

Clone "vb2\_1"

A polynucleotide of the present invention has been identified as clone "vb2\_1".  
10 vb2\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb2\_1 protein").

The nucleotide sequence of vb2\_1 as presently determined is reported in SEQ ID  
15 NO:1, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:2. Amino acids 15 to 27 of SEQ ID NO:2 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted  
20 leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb2\_1 protein.

If a frameshift were introduced into the nucleotide sequence of SEQ ID NO:1 by deleting one of the adenine residues at positions 315 and 316, another potential vb2\_1 reading frame and predicted amino acid sequence could be encoded by basepairs 126 to  
25 381 of SEQ ID NO:1 and is reported in SEQ ID NO:97. Amino acids 15 to 27 of SEQID NO:97 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28 of SEQ ID NO:97, or are a transmembrane domain.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone  
vb2\_1 should be approximately 2342 bp.

30 The nucleotide sequence disclosed herein for vb2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb2\_1 demonstrated at least some similarity with sequences identified as AA308563 (EST179381 HCC cell line (metastasis to liver in mouse) II Homo

sapiens cDNA 5' end, mRNA sequence). Based upon sequence similarity, vb2\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "vb3\_1"

5 A polynucleotide of the present invention has been identified as clone "vb3\_1". vb3\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb3\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb3\_1 protein").

10 The nucleotide sequence of vb3\_1 as presently determined is reported in SEQ ID NO:3, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb3\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:4. Amino acids 16 to 28 of SEQ ID NO:4 are a predicted leader/signal sequence, with the predicted mature amino 15 acid sequence beginning at amino acid 29. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb3\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb3\_1 should be approximately 2498 bp.

20 The nucleotide sequence disclosed herein for vb3\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb3\_1 demonstrated at least some similarity with sequences identified as AA098874 (zn45f11.s1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 550413 3', mRNA sequence) and T26482 (Human gene signature HUMGS08724). 25 Based upon sequence similarity, vb3\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "vb4\_1"

A polynucleotide of the present invention has been identified as clone "vb4\_1". 30 vb4\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb4\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb4\_1 protein").

The nucleotide sequence of vb4\_1 as presently determined is reported in SEQ ID NO:5, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb4\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:6. Amino acids 2 to 14 of 5 SEQ ID NO:6 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb4\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone 10 vb4\_1 should be approximately 2161 bp.

The nucleotide sequence disclosed herein for vb4\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb4\_1 demonstrated at least some similarity with sequences identified as D88035 (Rat mRNA for glycoprotein specific UDP-glucuronyltransferase, 15 complete cds), N49234 (yy83b10.s1 Homo sapiens cDNA clone 280123 3'), and Q59845 (Human brain Expressed Sequence Tag EST00765). Based upon sequence similarity, vb4\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vb4\_1 protein sequence, one centered around amino acid 40 and another 20 around amino acid 80 of SEQ ID NO:6.

#### Clone "vb5\_1"

A polynucleotide of the present invention has been identified as clone "vb5\_1". vb5\_1 was isolated from a human fetal brain cDNA library and was identified as encoding 25 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb5\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb5\_1 protein").

The nucleotide sequence of vb5\_1 as presently determined is reported in SEQ ID NO:7, and includes a poly(A) tail. What applicants presently believe to be the proper 30 reading frame and the predicted amino acid sequence of the vb5\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:8. Amino acids 7 to 19 of SEQ ID NO:8 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the hydrophobic nature of the predicted

leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb5\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb5\_1 should be approximately 724 bp.

5 The nucleotide sequence disclosed herein for vb5\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb5\_1 demonstrated at least some similarity with sequences identified as AA835218 (ak65a05.s1 Barstead pancreas HPLRB1 Homo sapiens cDNA clone IMAGE:1412720 3', mRNA sequence). Based upon sequence similarity, vb5\_1  
10 proteins and each similar protein or peptide may share at least some activity.

#### Clone "vb6\_1"

A polynucleotide of the present invention has been identified as clone "vb6\_1". vb6\_1 was isolated from a human fetal brain cDNA library and was identified as encoding 15 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb6\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb6\_1 protein").

The nucleotide sequence of vb6\_1 as presently determined is reported in SEQ ID NO:9, and includes a poly(A) tail. What applicants presently believe to be the proper 20 reading frame and the predicted amino acid sequence of the vb6\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. Amino acids 13 to 25 of SEQ ID NO:10 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 25 the predicted leader/signal sequence not be separated from the remainder of the vb6\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb6\_1 should be approximately 2685 bp.

The nucleotide sequence disclosed herein for vb6\_1 was searched against the 30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb6\_1 demonstrated at least some similarity with sequences identified as AA478801 (zv20f05.s1 Soares NhHMPu S1 Homo sapiens cDNA clone

754209 3', mRNA sequence). Based upon sequence similarity, vb6\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "vb7\_1"

5 A polynucleotide of the present invention has been identified as clone "vb7\_1". vb7\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb7\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb7\_1 protein").

10 The nucleotide sequence of vb7\_1 as presently determined is reported in SEQ ID NO:11, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb7\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 35 to 47 of SEQ ID NO:12 are a predicted leader/signal sequence, with the predicted mature 15 amino acid sequence beginning at amino acid 48. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb7\_1 protein.

Another potential vb7\_1 reading frame and predicted amino acid sequence that 20 could be encoded by basepairs 1093 to 1577 of SEQ ID NO:11 is reported in SEQ ID NO:98. Amino acids 11 to 23 of SEQ ID NO:98 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24 of SEQ ID NO:98, or are a transmembrane domain. The TopPredII computer program predicts 25 another potential transmembrane domain within the protein sequence of SEQ ID NO:98 centered around amino acid 86 of SEQ ID NO:98. If a frameshift were introduced into the nucleotide sequence of SEQ ID NO:11 approximately between position 1090 and position 1253, the open reading frame of SEQ ID NO:12 could be joined to the open reading frame of SEQ ID NO:98.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone 30 vb7\_1 should be approximately 1730 bp.

The nucleotide sequence disclosed herein for vb7\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb7\_1 demonstrated at least some similarity with sequences identified as D13748 (human eukaryotic initiation factor 4AI), M22873 (Mus musculus

protein synthesis initiation factor 4A (eIF-4A) gene, exon 1), and N36589 (yx86f08.r1 Homo sapiens cDNA clone 268647 5'). The predicted amino acid sequence disclosed herein for vb7\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vb7\_1 protein demonstrated 5 at least some similarity to the sequence identified as AL021839 (hypothetical protein [Schizosaccharomyces pombe]). Based upon sequence similarity, vb7\_1 proteins and each similar protein or peptide may share at least some activity.

vb7\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 45 kDa was detected in membrane fractions using SDS 10 polyacrylamide gel electrophoresis.

Clone "vb8\_1"

A polynucleotide of the present invention has been identified as clone "vb8\_1". vb8\_1 was isolated from a human fetal brain cDNA library and was identified as encoding 15 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb8\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb8\_1 protein").

The nucleotide sequence of vb8\_1 as presently determined is reported in SEQ ID NO:13, and includes a poly(A) tail. What applicants presently believe to be the proper 20 reading frame and the predicted amino acid sequence of the vb8\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:14.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb8\_1 should be approximately 1363 bp.

The nucleotide sequence disclosed herein for vb8\_1 was searched against the 25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb8\_1 demonstrated at least some similarity with sequences identified as N57252 (yw93d11.r1 Homo sapiens cDNA clone 259797 5'). The predicted amino acid sequence disclosed herein for vb8\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The 30 predicted vb8\_1 protein demonstrated at least some similarity to sequences identified as AF51239 (probable ubiquitin activating enzyme 2 [Picea mariana]). Based upon sequence similarity, vb8\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain

within the vb8\_1 protein sequence centered around amino acid 30 of SEQ ID NO:14. Both the CodonPreference and Testcode computer programs indicate that frameshifts in the nucleotide sequence of SEQ ID NO:13, resulting in the joining of the open reading frame of SEQ ID NO:14 with open reading frames that are more 5' to that of SEQ ID NO:14, are 5 likely.

vb8\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 23 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

10 Clone "vb9\_1"

A polynucleotide of the present invention has been identified as clone "vb9\_1". vb9\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb9\_1 is a full-length clone, including the entire coding 15 sequence of a secreted protein (also referred to herein as "vb9\_1 protein").

The nucleotide sequence of vb9\_1 as presently determined is reported in SEQ ID NO:15, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb9\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:16. Amino acids 3 to 15 20 of SEQ ID NO:16 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 16. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb9\_1 protein.

25 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb9\_1 should be approximately 2996 bp.

The nucleotide sequence disclosed herein for vb9\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb9\_1 demonstrated at least some similarity with sequences 30 identified as AA446380 (zw58b09.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 774233 5', mRNA sequence) and L48440 (Rattus norvegicus collagen type II mRNA, complete cds). The predicted amino acid sequence disclosed herein for vb9\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the

BLASTX search protocol. The predicted vb9\_1 protein demonstrated at least some similarity to the sequence identified as Z78279 (Collagen alpha1 [Rattus norvegicus]). Based upon sequence similarity, vb9\_1 proteins and each similar protein or peptide may share at least some activity.

5 vb9\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 58 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "vc3\_1"

10 A polynucleotide of the present invention has been identified as clone "vc3\_1". vc3\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc3\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc3\_1 protein").

15 The nucleotide sequence of vc3\_1 as presently determined is reported in SEQ ID NO:17, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc3\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:18. Amino acids 24 to 36 of SEQ ID NO:18 are a predicted leader/signal sequence, with the predicted mature 20 amino acid sequence beginning at amino acid 37. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc3\_1 protein.

Another potential vc3\_1 reading frame and predicted amino acid sequence is 25 encoded by basepairs 227 to 703 of SEQ ID NO:17 and is reported in SEQ ID NO:99. Amino acids 83 to 95 of SEQ ID NO:99 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 96, or are a transmembrane domain, and the TopPredII computer program predicts two additional 30 transmembrane domains within the SEQ ID NO:99 amino acid sequence. A frameshift in the nucleotide sequence of SEQ ID NO:17 between about nucleotide 109 to about nucleotide 417 could join together portions of the overlapping reading frames of SEQ ID NO:18 and SEQ ID NO:99.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc3\_1 should be approximately 950 bp.

The nucleotide sequence disclosed herein for vc3\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 5 FASTA search protocols. vc3\_1 demonstrated at least some similarity with sequences identified as AA669665 (ac18h12.s1 Stratagene ovary (#937217) Homo sapiens cDNA clone 856871 3'). Based upon sequence similarity, vc3\_1 proteins and each similar protein or peptide may share at least some activity.

vc3\_1 protein was expressed in a COS cell expression system, and an expressed 10 protein band of approximately 19 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "vc4\_1"

A polynucleotide of the present invention has been identified as clone "vc4\_1". 15 vc4\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc4\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc4\_1 protein").

The nucleotide sequence of vc4\_1 as presently determined is reported in SEQ ID 20 NO:19, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc4\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:20. Amino acids 2 to 14 of SEQ ID NO:20 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the 25 predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc4\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc4\_1 should be approximately 1200 bp.

30 The nucleotide sequence disclosed herein for vc4\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc4\_1 demonstrated at least some similarity with sequences identified as Q40970 (Human skeletal muscle ADP-ribosyltransferase gene), U60881 (Mus musculus Yac-2 NAD:arginine ADP-ribosyltransferase mRNA, complete cds), and

W12489 (ma57b11.r1 Soares mouse p3NMF19.5 Mus musculus cDNA clone 314781 5' similar to SW RT61\_RAT P17982 ALLOANTIGEN RT6.1 PRECURSOR). The predicted amino acid sequence disclosed herein for vc4\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The 5 predicted vc4\_1 protein demonstrated at least some similarity to sequences identified as R37572 (Rabbit skeletal muscle ADP-ribosyltransferase) and U60881 (Yac-2 NAD arginine ADP-ribosyltransferase [Mus musculus]). ADP-ribosyltransferases are localized to the plasma membrane and are involved in "post-translational modification of proteins in which the ADP-ribose moiety of NAD is transferred to proteins", which is "responsible 10 for the toxicity of some bacterial toxins (e.g. cholera toxin and pertussis toxin)". Based upon sequence similarity, vc4\_1 proteins and each similar protein or peptide may share at least some activity.

vc4\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 26 kDa was detected in membrane fractions using SDS 15 polyacrylamide gel electrophoresis.

Clone "vc5\_1"

A polynucleotide of the present invention has been identified as clone "vc5\_1". vc5\_1 was isolated from a human fetal brain cDNA library and was identified as encoding 20 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc5\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc5\_1 protein").

The nucleotide sequence of vc5\_1 as presently determined is reported in SEQ ID NO:21, and includes a poly(A) tail. What applicants presently believe to be the proper 25 reading frame and the predicted amino acid sequence of the vc5\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:22. Amino acids 63 to 75 of SEQ ID NO:22 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 76. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 30 the predicted leader/signal sequence not be separated from the remainder of the vc5\_1 protein.

Another potential vc5\_1 reading frame and predicted amino acid sequence is encoded by basepairs 215-376 of SEQ ID NO:21 and is reported in SEQ ID NO:100. Amino

acids 4 to 16 of SEQ ID NO:100 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17 of SEQ ID NO:100.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc5\_1 should be approximately 1650 bp.

5 The nucleotide sequence disclosed herein for vc5\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc5\_1 demonstrated at least some similarity with sequences identified as AA002211 (zh81h07.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 427741 3'). Based upon sequence similarity, vc5\_1 proteins and each similar 10 protein or peptide may share at least some activity.

vc5\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 28 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

15 Clone "vc7\_1"

A polynucleotide of the present invention has been identified as clone "vc7\_1". vc7\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc7\_1 is a full-length clone, including the entire coding 20 sequence of a secreted protein (also referred to herein as "vc7\_1 protein").

The nucleotide sequence of vc7\_1 as presently determined is reported in SEQ ID NO:23, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc7\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino acids 11 to 23 25 of SEQ ID NO:24 are a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc7\_1 should be approximately 2600 bp.

The nucleotide sequence disclosed herein for vc7\_1 was searched against the 30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database.

Clone "vc9\_1"

A polynucleotide of the present invention has been identified as clone "vc9\_1". vc9\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid 5 sequence of the encoded protein. vc9\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc9\_1 protein").

The nucleotide sequence of vc9\_1 as presently determined is reported in SEQ ID NO:25, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc9\_1 protein corresponding 10 to the foregoing nucleotide sequence is reported in SEQ ID NO:26. Amino acids 10 to 22 of SEQ ID NO:26 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc9\_1 15 protein.

Another potential vc9\_1 reading frame and predicted amino acid sequence is encoded by basepairs 1981 to 2619 of SEQ ID NO:25 and is reported in SEQ ID NO:101.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc9\_1 should be approximately 4500 bp.

20 The nucleotide sequence disclosed herein for vc9\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc9\_1 demonstrated at least some similarity with sequences identified as N66453 (yz41a08.s1 Homo sapiens cDNA clone 285590 3') and Z75407 (Human DNA sequence from cosmid N128A12 on chromosome 22q12-qter contains ESTs, 25 CpG island). Based upon sequence similarity, vc9\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vc9\_1 protein sequence at the extreme C-terminus of SEQ ID NO:26.

30 Clone "vc10\_1"

A polynucleotide of the present invention has been identified as clone "vc10\_1". vc10\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the

amino acid sequence of the encoded protein. vc10\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc10\_1 protein").

The nucleotide sequence of vc10\_1 as presently determined is reported in SEQ ID NO:27, and includes a poly(A) tail. What applicants presently believe to be the proper 5 reading frame and the predicted amino acid sequence of the vc10\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:28. Amino acids 21 to 33 of SEQ ID NO:28 are a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 34.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone 10 vc10\_1 should be approximately 2600 bp.

The nucleotide sequence disclosed herein for vc10\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc10\_1 demonstrated at least some similarity with sequences identified as AA398711 (zt75a05.s1 Soares testis NHT Homo sapiens cDNA clone 728144 15 3') and T24621 (Human gene signature HUMGS06681). Based upon sequence similarity, vc10\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vc10\_1 protein sequence centered around amino acid 74 of SEQ ID NO:28. Nucleotides 1103 to 1191 of SEQ ID NO:27 represent a possible intron in the predicted 3' untranslated 20 region of the vc10\_1 mRNA molecule.

#### Clone "vc11\_1"

A polynucleotide of the present invention has been identified as clone "vc11\_1". vc11\_1 was isolated from a human fetal brain cDNA library and was identified as 25 encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc11\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc11\_1 protein").

The nucleotide sequence of vc11\_1 as presently determined is reported in SEQ ID NO:29, and includes a poly(A) tail. What applicants presently believe to be the proper 30 reading frame and the predicted amino acid sequence of the vc11\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:30. Amino acids 6 to 18 of SEQ ID NO:30 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the vc11\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc11\_1 should be approximately 2600 bp.

5 The nucleotide sequence disclosed herein for vc11\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc11\_1 demonstrated at least some similarity with sequences identified as AA193348 (zr41c08.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 665966 5') and T23590 (Human gene signature HUMGS05443). Based upon sequence similarity,  
10 vc11\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vc11\_1 protein sequence centered around amino acid 32 of SEQ ID NO:30.

Clone "vc14\_1"

15 A polynucleotide of the present invention has been identified as clone "vc14\_1". vc14\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc14\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc14\_1 protein").

20 The nucleotide sequence of vc14\_1 as presently determined is reported in SEQ ID NO:31, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc14\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:32. Amino acids 21 to 33 of SEQ ID NO:32 are a predicted leader/signal sequence, with the predicted mature  
25 amino acid sequence beginning at amino acid 34. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc14\_1 protein.

30 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc14\_1 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for vc14\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc14\_1 demonstrated at least some similarity with sequences identified as AA258182 (zs35f09.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE

687209 3'). The predicted amino acid sequence disclosed herein for vc14\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc14\_1 protein demonstrated at least some similarity to sequences identified as AC002339 (BAC T11A7 [Arabidopsis thaliana]) and Z71266 5 (R06C7.6 [Caenorhabditis elegans]). Based upon sequence similarity, vc14\_1 proteins and each similar protein or peptide may share at least some activity.

vc14\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 22 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

10

Clone "vc16\_1"

A polynucleotide of the present invention has been identified as clone "vc16\_1". vc16\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the 15 amino acid sequence of the encoded protein. vc16\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc16\_1 protein").

The nucleotide sequence of vc16\_1 as presently determined is reported in SEQ ID NO:33, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc16\_1 protein corresponding 20 to the foregoing nucleotide sequence is reported in SEQ ID NO:34. Amino acids 15 to 27 of SEQ ID NO:34 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 25 the predicted leader/signal sequence not be separated from the remainder of the vc16\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc16\_1 should be approximately 1256 bp.

The nucleotide sequence disclosed herein for vc16\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 30 FASTA search protocols. vc16\_1 demonstrated at least some similarity with sequences identified as AA776882 (ac40a09.s1 Stratagene hNT neuron (#937233) Homo sapiens cDNA clone 858904 3' similar to SW XB3\_XENLA Q09004 STATHMIN-LIKE PROTEIN XB3, mRNA sequence), AF026528 (Rattus norvegicus stathmin-like-protein

RB3 mRNA, complete cds), and AF026529 (Rattus norvegicus stathmin-like-protein splice variant RB3' mRNA, complete cds). The predicted amino acid sequence disclosed herein for vc16\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc16\_1 protein demonstrated at least 5 some similarity to sequences identified as AF026528 (stathmin-like-protein RB3 [Rattus norvegicus]). While stathmin itself is intracellular, stathmin-related protein RB3 (as well as related proteins SCG10 in rat and XB3 in *Xenopus*) is membrane-associated and has been isolated in the membrane fraction from cell cultures. RB3 is expressed in neural tissue and may be involved in the expression of differentiated neuronal function. Based 10 upon sequence similarity, vc16\_1 proteins and each similar protein or peptide may share at least some activity.

vc16\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 89 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

15

Clone "vc17\_1"

A polynucleotide of the present invention has been identified as clone "vc17\_1". vc17\_1 was isolated from a human fetal brain cDNA library and was identified as 20 encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc17\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc17\_1 protein").

The nucleotide sequence of vc17\_1 as presently determined is reported in SEQ ID NO:35, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc17\_1 protein corresponding 25 to the foregoing nucleotide sequence is reported in SEQ ID NO:36. Amino acids 30 to 42 of SEQ ID NO:36 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc17\_1 30 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc17\_1 should be approximately 1783 bp.

The nucleotide sequence disclosed herein for vc17\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc17\_1 demonstrated at least some similarity with sequences identified as N73805 (yz80g02.s1 Homo sapiens cDNA clone 289394 3'), and T24437 5 (Human gene signature HUMGS06471). Based upon sequence similarity, vc17\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vc17\_1 protein sequence centered around amino acid 60 of SEQ ID NO:36.

10 Clone "vc21\_1"

A polynucleotide of the present invention has been identified as clone "vc21\_1". vc21\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc21\_1 is a full-length clone, including the 15 entire coding sequence of a secreted protein (also referred to herein as "vc21\_1 protein").

The nucleotide sequence of vc21\_1 as presently determined is reported in SEQ ID NO:37, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc21\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:38. Amino acids 11 to 23 20 of SEQ ID NO:38 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc21\_1 protein.

25 Another potential vc21\_1 reading frame and predicted amino acid sequence is encoded by basepairs 796 to 1014 of SEQ ID NO:37 and is reported in SEQ ID NO:102.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc21\_1 should be approximately 1773 bp.

The nucleotide sequence disclosed herein for vc21\_1 was searched against the 30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc21\_1 demonstrated at least some similarity with sequences identified as W85910 (zh52b10.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 415675 3', mRNA sequence) and T24609 (Human gene signature

HUMGS06668). Based upon sequence similarity, vc21\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "vc23\_1"

5 A polynucleotide of the present invention has been identified as clone "vc23\_1". vc23\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc23\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc23\_1 protein").

10 The nucleotide sequence of vc23\_1 as presently determined is reported in SEQ ID NO:39, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc23\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:40. Amino acids 28 to 40 of SEQ ID NO:40 are a predicted leader/signal sequence, with the predicted mature 15 amino acid sequence beginning at amino acid 41. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc23\_1 protein.

20 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc23\_1 should be approximately 1998 bp.

The nucleotide sequence disclosed herein for vc23\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc23\_1 demonstrated at least some similarity with sequences identified as AA580484 (nn22a05.s1 NCI\_CGAP\_Co12 Homo sapiens cDNA clone 25 IMAGE:1084592 similar to TR:G1209718 G1209718 HYPOTHETICAL 50.1 KD PROTEIN, mRNA sequence), T25530 (Human gene signature HUMGS07700), U41293 (Saccharomyces cerevisiae putative serine/threonine protein kinase gene, putative ribosomal protein L25 gene, and malate dehydrogenase (MDH2) gene, complete cds), and Z74866 (S.cerevisiae chromosome XV reading frame ORF YOL124c). The predicted 30 amino acid sequence disclosed herein for vc23\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc23\_1 protein demonstrated at least some similarity to sequences identified as U41293 (unknown [Saccharomyces cerevisiae]) and Z74866 (ORF YOL124c [Saccharo-

myces cerevisiae]). Based upon sequence similarity, vc23\_1 proteins and each similar protein or peptide may share at least some activity. The vc23\_1 protein contains a "N-6 adenine-specific DNA methylases signature" motif. The TopPredII computer program predicts a potential transmembrane domain within the vc23\_1 protein sequence centered 5 around amino acid 232 of SEQ ID NO:40.

vc23\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 51 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

10 Clone "vc25\_1"

A polynucleotide of the present invention has been identified as clone "vc25\_1". vc25\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc25\_1 is a full-length clone, including the 15 entire coding sequence of a secreted protein (also referred to herein as "vc25\_1 protein").

The nucleotide sequence of vc25\_1 as presently determined is reported in SEQ ID NO:41, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc25\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:42. Amino acids 25 to 37 20 of SEQ ID NO:42 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 38. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc25\_1 protein.

25 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc25\_1 should be approximately 1653 bp.

The nucleotide sequence disclosed herein for vc25\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc25\_1 demonstrated at least some similarity with sequences 30 identified as N21690 (yx63h08.s1 Soares melanocyte 2NbHM Homo sapiens cDNA clone 266463 3', mRNA sequence) and T25257 (Human gene signature HUMGS07418). Based upon sequence similarity, vc25\_1 proteins and each similar protein or peptide may share at least some activity.

vc25\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 15 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

5 Clone "vc26\_1"

A polynucleotide of the present invention has been identified as clone "vc26\_1". vc26\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc26\_1 is a full-length clone, including the 10 entire coding sequence of a secreted protein (also referred to herein as "vc26\_1 protein").

The nucleotide sequence of vc26\_1 as presently determined is reported in SEQ ID NO:43, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc26\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:44. Amino acids 11 to 23 15 of SEQ ID NO:44 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc26\_1 protein.

20 If the "G" residue at position 669 of SEQ ID NO:43 were deleted to create a frameshift, another potential vc26\_1 reading frame and predicted amino acid sequence could be encoded by what would then be basepairs 87 to 992 of the deletion-containing version of SEQ ID NO:43. This potential vc26\_1 reading frame and predicted amino acid sequence is reported in SEQ ID NO:103. Amino acids 11 to 23 of both SEQ ID NO:44 and 25 SEQ ID NO:103 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24, or are a transmembrane domain.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc26\_1 should be approximately 1982 bp.

30 The nucleotide sequence disclosed herein for vc26\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc26\_1 demonstrated at least some similarity with sequences identified as AA877534 (nr01g08.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA clone IMAGE:1160606 3', mRNA sequence) and T25645 (Human gene signature HUMGS07835). The predicted vc26\_1 protein of SEQ ID NO:10 contains an immuno-

globulins and major histocompatibility complex proteins signature at amino acid 131. Based upon sequence similarity, vc26\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts seven additional potential transmembrane domains within the vc26\_1 protein sequence, centered around 5 amino acids 60, 100, 120, 160, 210, 250, and 290 of SEQ ID NO:44, respectively.

Clone "vc30\_1"

A polynucleotide of the present invention has been identified as clone "vc30\_1". vc30\_1 was isolated from a human fetal brain cDNA library and was identified as 10 encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc30\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc30\_1 protein").

The nucleotide sequence of vc30\_1 as presently determined is reported in SEQ ID NO:45, and includes a poly(A) tail. What applicants presently believe to be the proper 15 reading frame and the predicted amino acid sequence of the vc30\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:46. Amino acids 19 to 31 of SEQ ID NO:46 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 20 the predicted leader/signal sequence not be separated from the remainder of the vc30\_1 protein.

If a frameshift were introduced in the nucleotide sequence of SEQ ID NO:45 by deleting the cytosine residue at position 1393, another potential vc30\_1 reading frame and predicted amino acid sequence could be encoded by what would then be basepairs 1317 25 to 1659 of SEQ ID NO:45 and is reported in SEQ ID NO:104.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc30\_1 should be approximately 1887 bp.

The nucleotide sequence disclosed herein for vc30\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 30 FASTA search protocols. vc30\_1 demonstrated at least some similarity with sequences identified as AA496421 (zv37c04.r1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 755814 5', mRNA sequence). The predicted amino acid sequence disclosed herein for vc30\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc30\_1 protein demonstrated at least

some similarity to sequences identified as AF047760 (phosphatidic acid phosphohydrolase type 2c [Homo sapiens]). Based upon sequence similarity, vc30\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vc30\_1 5 protein sequence centered around amino acid 55 of SEQ ID NO:46.

Clone "vd1\_1"

A polynucleotide of the present invention has been identified as clone "vd1\_1". vd1\_1 was isolated from a human adult skin cDNA library and was identified as encoding 10 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vd1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vd1\_1 protein").

The nucleotide sequence of vd1\_1 as presently determined is reported in SEQ ID NO:47, and includes a poly(A) tail. What applicants presently believe to be the proper 15 reading frame and the predicted amino acid sequence of the vd1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:48. Amino acids 8 to 20 of SEQ ID NO:48 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 20 the predicted leader/signal sequence not be separated from the remainder of the vd1\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vd1\_1 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for vd1\_1 was searched against the 25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vd1\_1 demonstrated at least some similarity with sequences identified as AA582963 (nn72e02.s1 NCI\_CGAP\_Lar1 Homo sapiens cDNA clone IMAGE 1089434) and AC002389 (Human DNA from chromosome 19 specific cosmid R28461, genomic sequence, complete sequence). Based upon sequence similarity, vd1\_1 proteins 30 and each similar protein or peptide may share at least some activity. There is an 18-residue amino acid stretch (with an approximate consensus sequence shown in SEQ ID NO:105 (HHAAGQAGNEAGRFGQGV)) that is almost tandemly repeated 15 times in the vd1\_1 protein. Nucleotides 406-1668 of SEQ ID NO:47, which encode a region of SEQ ID

NO:48 that includes the 18-residue amino acid repeats, may represent an alternatively spliced region in mRNA molecules transcribed from the vd1\_1 gene.

vd1\_protein was expressed in a COS cell expression system, and an expressed protein band of approximately 55 kDa was detected in conditioned medium using SDS

5 polyacrylamide gel electrophoresis.

Clone "vd2\_1"

A polynucleotide of the present invention has been identified as clone "vd2\_1". vd2\_1 was isolated from a human adult skin cDNA library and was identified as encoding

10 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vd2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vd2\_1 protein").

The nucleotide sequence of vd2\_1 as presently determined is reported in SEQ ID NO:49, and includes a poly(A) tail. What applicants presently believe to be the proper

15 reading frame and the predicted amino acid sequence of the vd2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:50. Amino acids 2 to 14 of SEQ ID NO:50 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

20 the predicted leader/signal sequence not be separated from the remainder of the vd2\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vd2\_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for vd2\_1 was searched against the

25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vd2\_1 demonstrated at least some similarity with sequences identified as H03945 (yJ44c02.s1 Homo sapiens cDNA clone 151586 3'). Based upon sequence similarity, vd2\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane

30 domain within the vd2\_1 protein sequence centered around amino acid 115 of SEQ ID NO:50.

Clone "vd3\_1"

A polynucleotide of the present invention has been identified as clone "vd3\_1". vd3\_1 was isolated from a human adult skin cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid 5 sequence of the encoded protein. vd3\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vd3\_1 protein").

The nucleotide sequence of vd3\_1 as presently determined is reported in SEQ ID NO:51, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vd3\_1 protein corresponding 10 to the foregoing nucleotide sequence is reported in SEQ ID NO:52. Amino acids 5 to 17 of SEQ ID NO:52 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 18. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vd3\_1 15 protein.

If a frameshift were introduced into the nucleotide sequence of SEQ ID NO:19 by inserting an adenine or thymine residue at position 1132 or 1133, another potential vd3\_1 reading frame and predicted amino acid sequence could be encoded by basepairs 176 to 20 1281 of SEQ ID NO:51 and is reported in SEQ ID NO:106. Amino acids 5 to 17 of SEQID NO:106 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 18 of SEQ ID NO:106, or are a transmembrane domain.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vd3\_1 should be approximately 1537 bp.

The nucleotide sequence disclosed herein for vd3\_1 was searched against the 25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vd3\_1 demonstrated at least some similarity with sequences identified as AA873028 (ob11e05.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA clone IMAGE 1323392 3', mRNA sequence), AC002389 (Human DNA from chromosome 19 specific cosmid R28461, genomic sequence, complete sequence), and AD001502 (Homo 30 sapiens DNA from chromosome 19-cosmid f21246, genomic sequence). Based upon sequence similarity, vd3\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional possible transmembrane domain within the vd3\_1 protein sequence centered around amino acid

290 of SEQ ID NO:52. The vd3\_1 protein is apparently a splice variant of the vd4\_1 protein described below.

vd3\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 42 kDa was detected in membrane fractions using SDS 5 polyacrylamide gel electrophoresis.

Clone "vd4\_1"

A polynucleotide of the present invention has been identified as clone "vd4\_1". vd4\_1 was isolated from a human adult skin cDNA library and was identified as encoding 10 a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vd4\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vd4\_1 protein").

The nucleotide sequence of vd4\_1 as presently determined is reported in SEQ ID NO:53, and includes a poly(A) tail. What applicants presently believe to be the proper 15 reading frame and the predicted amino acid sequence of the vd4\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:54. Amino acids 5 to 17 of SEQ ID NO:54 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 18. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 20 the predicted leader/signal sequence not be separated from the remainder of the vd4\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vd4\_1 should be approximately 1897 bp.

The nucleotide sequence disclosed herein for vd4\_1 was searched against the 25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vd4\_1 demonstrated at least some similarity with sequences identified as AA706316 (ah28e11.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 1240172 3', mRNA sequence), AC002389 (Human DNA from chromosome 19 specific cosmid R28461, genomic sequence, complete sequence), and AD001502 30 (Homo sapiens DNA from chromosome 19-cosmid f21246, genomic sequence). Based upon sequence similarity, vd4\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional possible transmembrane domain within the vd4\_1 protein sequence centered around amino acid

290 of SEQ ID NO:54. The vd4\_1 protein is apparently a splice variant of the vd3\_1 protein described above.

vd4\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 54 kDa was detected in conditioned medium using SDS 5 polyacrylamide gel electrophoresis.

Clone "ve4\_1"

A polynucleotide of the present invention has been identified as clone "ve4\_1". ve4\_1 was isolated from a human adult brain (Alzheimer's hippocampus level 7) cDNA 10 library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ve4\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ve4\_1 protein").

The nucleotide sequence of ve4\_1 as presently determined is reported in SEQ ID 15 NO:55, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ve4\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Amino acids 25 to 37 of SEQ ID NO:56 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 38. Due to the hydrophobic nature of the 20 predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ve4\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ve4\_1 should be approximately 1578 bp.

25 The nucleotide sequence disclosed herein for ve4\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ve4\_1 demonstrated at least some similarity with sequences identified as AA707153 (zj33f10.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 452107 3' similar to TR P70295 P70295 AUP1 PRECURSOR, mRNA 30 sequence) and U41736 (Mus musculus ancient ubiquitous 46 kDa protein AUP1 precursor (Aup1) mRNA, complete cds). The predicted amino acid sequence disclosed herein for ve4\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ve4\_1 protein demonstrated at least

some similarity to the sequence identified as U41736 (ancient ubiquitous 46 kDa protein AUP46 precursor [Mus musculus]). Based upon sequence similarity, ve4\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the ve4\_1 5 protein sequence, one centered around amino acid 110 and another around amino acid 210 of SEQ ID NO:56.

ve4\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 41 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

10

Clone "ve8\_1"

A polynucleotide of the present invention has been identified as clone "ve8\_1". ve8\_1 was isolated from a human adult brain (Alzheimer's hippocampus level 7) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis 15 of computer analysis of the amino acid sequence of the encoded protein. ve8\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ve8\_1 protein").

The nucleotide sequence of ve8\_1 as presently determined is reported in SEQ ID NO:57, and includes a poly(A) tail. What applicants presently believe to be the proper 20 reading frame and the predicted amino acid sequence of the ve8\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:58. Amino acids 18 to 30 of SEQ ID NO:58 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 31. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should 25 the predicted leader/signal sequence not be separated from the remainder of the ve8\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ve8\_1 should be approximately 2093 bp.

The nucleotide sequence disclosed herein for ve8\_1 was searched against the 30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ve8\_1 demonstrated at least some similarity with sequences identified as AC004126 (Homo sapiens Chromosome 11q12 pac pDJ606g6; HTGS phase 1, 17 unordered pieces). Based upon sequence similarity, ve8\_1 proteins and each similar

protein or peptide may share at least some activity. The TopPredII computer program predicts four additional potential transmembrane domains within the ve8\_1 protein sequence, centered around amino acids 94, 147, 150, and 193 of SEQ ID NO:58, respectively.

5

Clone "vf1\_1"

A polynucleotide of the present invention has been identified as clone "vf1\_1". vf1\_1 was isolated from a human adult heart cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the 10 amino acid sequence of the encoded protein. vf1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vf1\_1 protein").

The nucleotide sequence of vf1\_1 as presently determined is reported in SEQ ID NO:59, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vf1\_1 protein corresponding 15 to the foregoing nucleotide sequence is reported in SEQ ID NO:60. Amino acids 13 to 25 of SEQ ID NO:60 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vf1\_1 20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vf1\_1 should be approximately 1382 bp.

The nucleotide sequence disclosed herein for vf1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 25 FASTA search protocols. vf1\_1 demonstrated at least some similarity with sequences identified as AA349531 (EST56314 Infant brain Homo sapiens cDNA 5' end, mRNA sequence) and AA532642 (nj17c07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA clone IMAGE 986604, mRNA sequence). Based upon sequence similarity, vf1\_1 proteins and 30 each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vf1\_1 protein sequence centered around amino acid 138 of SEQ ID NO:60.

vf1\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 40 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

5           Clone "vh1\_1"

A polynucleotide of the present invention has been identified as clone "vh1\_1". vh1\_1 was isolated from a human adult thymus cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vh1\_1 is a full-length clone, including the 10 entire coding sequence of a secreted protein (also referred to herein as "vh1\_1 protein").

The nucleotide sequence of vh1\_1 as presently determined is reported in SEQ ID NO:61, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vh1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:62. Amino acids 42 to 54 15 of SEQ ID NO:62 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 55. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vh1\_1 protein.

20           Another potential vh1\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 833 to 1054 of SEQ ID NO:61 is reported in SEQ ID NO:107. Amino acids 22 to 34 of SEQ ID NO:107 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 35 of SEQ ID NO:107, or are a transmembrane domain. If a frameshift were introduced into the 25 nucleotide sequence of SEQ ID NO:61 approximately between position 830 and position 998, the open reading frame of SEQ ID NO:62 could be joined to the open reading frame of SEQ ID NO:107.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vh1\_1 should be approximately 1529 bp.

30           The nucleotide sequence disclosed herein for vh1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vh1\_1 demonstrated at least some similarity with sequences identified as AA927736 (om72h10.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA clone

IMAGE:1552771 3', mRNA sequence). Based upon sequence similarity, vi1\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "vi1\_1"

5 A polynucleotide of the present invention has been identified as clone "vi1\_1". vi1\_1 was isolated from a human adult aorta cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vi1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vi1\_1 protein").

10 The nucleotide sequence of vi1\_1 as presently determined is reported in SEQ ID NO:63, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vi1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:64. Amino acids 13 to 25 of SEQ ID NO:64 are a predicted leader/signal sequence, with the predicted mature 15 amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vi1\_1 protein.

20 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vi1\_1 should be approximately 2348 bp.

The nucleotide sequence disclosed herein for vi1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vi1\_1 demonstrated at least some similarity with sequences identified as AA411541 (zv30a03.r1 Soares ovary tumor NbHOT Homo sapiens cDNA 25 clone 755116 5' similar to WP:F07H5.11 CE03160) and T21484 (Human gene signature HUMGS02856). The predicted amino acid sequence disclosed herein for vi1\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vi1\_1 protein demonstrated at least some similarity to the sequence identified as Z68314 (F46C5.9 [Caenorhabditis elegans]). The 30 amino acid sequence of the predicted vi1\_1 protein indicates that it may contain a beta-transducin family Trp-Asp repeat signature (WD-40) motif centered around residue 300 of SEQ ID NO:28. The WD-40 motif is thought to be a widely distributed protein-protein interaction domain. Based upon sequence similarity, vi1\_1 proteins and each similar

protein or peptide may share at least some activity. The TopPredII computer program predicts two additional possible transmembrane domains within the vi1\_1 protein sequence, one centered around amino acid 200 and another around amino acid 340 of SEQ ID NO:64.

5        vi1\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 45 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Deposit of Clones

10        Clones vc3\_1, vc4\_1, vc5\_1, vc7\_1, vc9\_1, vc10\_1, vc11\_1, vc14\_1, vd1\_1, and vd2\_1 were deposited on April 24, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98748, from which each clone comprising a particular polynucleotide is obtainable.

15        Clone vc21\_1 was deposited on June 10, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number ATCC 98785, from which each clone comprising a particular polynucleotide is obtainable.

20        Clones vc16\_1, vc17\_1, vc23\_1, vc25\_1, vc26\_1, ve4\_1, and vf1\_1 were deposited on June 10, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98784, from which each clone comprising a particular polynucleotide is obtainable.

25        Clones vb2\_1, vb3\_1, vb4\_1, vb5\_1, vb6\_1, vb7\_1, vb8\_1, vb9\_1, vc30\_1, vd3\_1, vd4\_1, ve8\_1, vh1\_1, and vi1\_1 were deposited on July 1, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98804, from which each clone comprising a particular polynucleotide is obtainable.

30        All restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent, except for the requirements specified in 37 C.F.R. § 1.808(b), and the term of the deposit will comply with 37 C.F.R. § 1.806.

Each clone has been transfected into separate bacterial cells (*E. coli*) in these composite deposits. Each clone can be removed from the vector in which it was deposited by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI) to produce the appropriate fragment for such clone. Each clone was deposited in either the pED6 or 5 pNOTs vector depicted in Figures 1A and 1B, respectively. The pED6dpc2 vector ("pED6") was derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning (Kaufman *et al.*, 1991, *Nucleic Acids Res.* **19**: 4485-4490); the pNOTs vector was derived from pMT2 (Kaufman *et al.*, 1989, *Mol. Cell. Biol.* **9**: 946-958) by deletion of the DHFR sequences, insertion of a new polylinker, and insertion of the M13 origin of 10 replication in the ClaI site. In some instances, the deposited clone can become "flipped" (i.e., in the reverse orientation) in the deposited isolate. In such instances, the cDNA insert can still be isolated by digestion with EcoRI and NotI. However, NotI will then produce the 5' site and EcoRI will produce the 3' site for placement of the cDNA in proper orientation for expression in a suitable vector. The cDNA may also be expressed from the 15 vectors in which they were deposited.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences 20 provided herein, or from a combination of those sequences. The sequence of an oligonucleotide probe that was used to isolate or to sequence each full-length clone is identified below, and should be most reliable in isolating the clone of interest.

	<u>Clone</u>	<u>Probe Sequence</u>
25	vb2_1	SEQ ID NO:65
	vb3_1	SEQ ID NO:66
	vb4_1	SEQ ID NO:67
	vb5_1	SEQ ID NO:68
	vb6_1	SEQ ID NO:69
30	vb7_1	SEQ ID NO:70
	vb8_1	SEQ ID NO:71
	vb9_1	SEQ ID NO:72
	vc3_1	SEQ ID NO:73
	vc4_1	SEQ ID NO:74

	vc5_1	SEQ ID NO:75
	vc7_1	SEQ ID NO:76
	vc9_1	SEQ ID NO:77
	vc10_1	SEQ ID NO:78
5	vc11_1	SEQ ID NO:79
	vc14_1	SEQ ID NO:80
	vc16_1	SEQ ID NO:81
	vc17_1	SEQ ID NO:82
	vc21_1	SEQ ID NO:83
10	vc23_1	SEQ ID NO:84
	vc25_1	SEQ ID NO:85
	vc26_1	SEQ ID NO:86
	vc30_1	SEQ ID NO:87
	vd1_1	SEQ ID NO:88
15	vd2_1	SEQ ID NO:89
	vd3_1	SEQ ID NO:90
	vd4_1	SEQ ID NO:91
	ve4_1	SEQ ID NO:92
	ve8_1	SEQ ID NO:93
20	vf1_1	SEQ ID NO:94
	vh1_1	SEQ ID NO:95
	vi1_1	SEQ ID NO:96

In the sequences listed above which include an N at position 2, that position is occupied  
25 in preferred probes/primers by a biotinylated phosphoaramidite residue rather than a nucleotide (such as, for example, that produced by use of biotin phosphoramidite (1-dimethoxytryloxy-2-(N-biotinyl-4-aminobutyl)-propyl-3-O-(2-cyanoethyl)-(N,N-diisopropyl)-phosphoramidite) (Glen Research, cat. no. 10-1953)).

The design of the oligonucleotide probe should preferably follow these  
30 parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) It should be designed to have a  $T_m$  of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).

The oligonucleotide should preferably be labeled with  $\gamma$ -<sup>32</sup>P ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established 5 methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4e+6 dpm/pmole.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100  $\mu$ l of the stock used to inoculate a sterile culture flask containing 25 ml 10 of sterile L-broth containing ampicillin at 100  $\mu$ g/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated 15 colonies on solid bacteriological media containing L-broth containing ampicillin at 100  $\mu$ g/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 20 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100  $\mu$ g/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1e+6 dpm/mL. The filter is then preferably 25 incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also 30 be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H.U. Saragovi, *et al.*, *Bio/Technology* 10, 773-778 (1992) and in R.S. 5 McDowell, *et al.*, *J. Amer. Chem. Soc.* 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker" sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion 10 could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decavalent form of the protein of the invention.

The present invention also provides both full-length and mature forms of the disclosed proteins. The full-length form of the such proteins is identified in the sequence 15 listing by translation of the nucleotide sequence of each disclosed clone. The mature form(s) of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with ATCC) in a suitable mammalian cell or other host cell. The sequence(s) of the mature form(s) of the protein may also be determinable from the amino acid sequence of the full-length form.

20 The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited 25 to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate 30 genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

The chromosomal location corresponding to the polynucleotide sequences disclosed herein may also be determined, for example by hybridizing appropriately

labeled polynucleotides of the present invention to chromosomes *in situ*. It may also be possible to determine the corresponding chromosomal location for a disclosed polynucleotide by identifying significantly similar nucleotide sequences in public databases, such as expressed sequence tags (ESTs), that have already been mapped to 5 particular chromosomal locations. For at least some of the polynucleotide sequences disclosed herein, public database sequences having at least some similarity to the polynucleotide of the present invention have been listed by database accession number. Searches using the GenBank accession numbers of these public database sequences can then be performed at an Internet site provided by the National Center for Biotechnology 10 Information having the address <http://www.ncbi.nlm.nih.gov/UniGene/>, in order to identify "UniGene clusters" of overlapping sequences. Many of the "UniGene clusters" so identified will already have been mapped to particular chromosomal sites.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The 15 desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, *Trends Pharmacol. Sci.* **15**(7): 250-254; Lavarosky *et al.*, 1997, *Biochem. Mol. Med.* **62**(1): 11-22; and Hampel, 1998, *Prog. Nucleic Acid Res. Mol. Biol.* **58**: 1-39; all of which are incorporated by reference herein). Transgenic animals that have 20 multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are 25 also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation 30 can be accomplished through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, *Bioessays* **14**(9): 629-633; Zwaal *et al.*, 1993, *Proc. Natl. Acad. Sci. USA* **90**(16): 7431-7435; Clark *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* **91**(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour *et al.*, 1988,

*Nature* 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614,396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for 5 the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s).

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms, part 10 or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information. For example, the TopPredII computer program can be used to predict the location of 15 transmembrane domains in an amino acid sequence, domains which are described by the location of the center of the transmsmbrane domain, with at least ten transmembrane amino acids on each side of the reported central residue(s).

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most 20 preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are 25 proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

In particular, sequence identity may be determined using WU-BLAST 30 (Washington University BLAST) version 2.0 software, which builds upon WU-BLAST version 1.4, which in turn is based on the public domain NCBI-BLAST version 1.4 (Altschul and Gish, 1996, Local alignment statistics, Doolittle *ed.*, *Methods in Enzymology* 266: 460-480; Altschul *et al.*, 1990, Basic local alignment search tool, *Journal of*

*Molecular Biology* **215**: 403-410; Gish and States, 1993, Identification of protein coding regions by database similarity search, *Nature Genetics* **3**: 266-272; Karlin and Altschul, 1993, Applications and statistics for multiple high-scoring segments in molecular sequences, *Proc. Natl. Acad. Sci. USA* **90**: 5873-5877; all of which are incorporated by reference herein). WU-BLAST version 2.0 executable programs for several UNIX platforms can be downloaded from <ftp://blast.wustl.edu/blast/executables>. The complete suite of search programs (BLASTP, BLASTN, BLASTX, TBLASTN, and TBLASTX) is provided at that site, in addition to several support programs. WU-BLAST 2.0 is copyrighted and may not be sold or redistributed in any form or manner without the express written consent of the author; but the posted executables may otherwise be freely used for commercial, nonprofit, or academic purposes. In all search programs in the suite -- BLASTP, BLASTN, BLASTX, TBLASTN and TBLASTX -- the gapped alignment routines are integral to the database search itself, and thus yield much better sensitivity and selectivity while producing the more easily interpreted output. Gapping can optionally be turned off in all of these programs, if desired. The default penalty (Q) for a gap of length one is Q=9 for proteins and BLASTP, and Q=10 for BLASTN, but may be changed to any integer value including zero, one through eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. The default per-residue penalty for extending a gap (R) is R=2 for proteins and BLASTP, and R=10 for BLASTN, but may be changed to any integer value including zero, one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. Any combination of values for Q and R can be used in order to align sequences so as to maximize overlap and identity while minimizing sequence gaps. The default amino acid comparison matrix is BLOSUM62, but other amino acid comparison matrices such as PAM can be utilized.

Species homologues of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide. Preferably, polynucleotide species homologues have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, and protein species homologues have at least 30% sequence

identity (more preferably, at least 45% identity; most preferably at least 60% identity) with the given protein, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides or the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Species homologues may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species. Preferably, species homologues are those isolated from mammalian species. Most preferably, species homologues are those isolated from certain mammalian species such as, for example, *Pan troglodytes*, *Gorilla gorilla*, *Pongo pygmaeus*, *Hylobates concolor*, *Macaca mulatta*, *Papio papio*, *Papio hamadryas*, *Cercopithecus aethiops*, *Cebus capucinus*, *Aotus trivirgatus*, *Sanguinus oedipus*, *Microcebus murinus*, *Mus musculus*, *Rattus norvegicus*, *Cricetus griseus*, *Felis catus*, *Mustela vison*, *Canis familiaris*, *Oryctolagus cuniculus*, *Bos taurus*, *Ovis aries*, *Sus scrofa*, and *Equus caballus*, for which genetic maps have been created allowing the identification of syntenic relationships between the genomic organization of genes in one species and the genomic organization of the related genes in another species (O'Brien and Seuánez, 1988, *Ann. Rev. Genet.* 22: 323-351; O'Brien *et al.*, 1993, *Nature Genetics* 3:103-112; Johansson *et al.*, 1995, *Genomics* 25: 682-690; Lyons *et al.*, 1997, *Nature Genetics* 15: 47-56; O'Brien *et al.*, 1997, *Trends in Genetics* 13(10): 393-399; Carver and Stubbs, 1997, *Genome Research* 7:1123-1137; all of which are incorporated by reference herein).

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotides which also encode proteins which are identical or have significantly similar sequences to those encoded by the disclosed polynucleotides. Preferably, allelic variants have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps. Allelic variants may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from individuals of the appropriate species.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides that hybridize under reduced stringency conditions, more preferably stringent conditions, and most preferably highly

stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least 5 stringent as, for example, conditions M-R.

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) <sup>†</sup>	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature and Buffer <sup>†</sup>
A	DNA:DNA	≥ 50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
B	DNA:DNA	<50	T <sub>B</sub> *; 1xSSC	T <sub>B</sub> *; 1xSSC
C	DNA:RNA	≥ 50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
D	DNA:RNA	<50	T <sub>D</sub> *; 1xSSC	T <sub>D</sub> *; 1xSSC
E	RNA:RNA	≥ 50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
F	RNA:RNA	<50	T <sub>F</sub> *; 1xSSC	T <sub>F</sub> *; 1xSSC
G	DNA:DNA	≥ 50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
H	DNA:DNA	<50	T <sub>H</sub> *; 4xSSC	T <sub>H</sub> *; 4xSSC
I	DNA:RNA	≥ 50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
J	DNA:RNA	<50	T <sub>J</sub> *; 4xSSC	T <sub>J</sub> *; 4xSSC
K	RNA:RNA	≥ 50	70°C; 4xSSC -or- 50°C; 4xSSC, 50% formamide	67°C; 1xSSC
L	RNA:RNA	<50	T <sub>L</sub> *; 2xSSC	T <sub>L</sub> *; 2xSSC
M	DNA:DNA	≥ 50	50°C; 4xSSC -or- 40°C; 6xSSC, 50% formamide	50°C; 2xSSC
N	DNA:DNA	<50	T <sub>N</sub> *; 6xSSC	T <sub>N</sub> *; 6xSSC
O	DNA:RNA	≥ 50	55°C; 4xSSC -or- 42°C; 6xSSC, 50% formamide	55°C; 2xSSC
P	DNA:RNA	<50	T <sub>P</sub> *; 6xSSC	T <sub>P</sub> *; 6xSSC
Q	RNA:RNA	≥ 50	60°C; 4xSSC -or- 45°C; 6xSSC, 50% formamide	60°C; 2xSSC
R	RNA:RNA	<50	T <sub>R</sub> *; 4xSSC	T <sub>R</sub> *; 4xSSC

<sup>†</sup>: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

<sup>†</sup>: SSPE (1xSSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

<sup>5</sup> \*T<sub>B</sub> - T<sub>R</sub>: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T<sub>m</sub>) of the hybrid, where T<sub>m</sub> is determined according to the following equations. For hybrids less than 18 base pairs in length, T<sub>m</sub>(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T<sub>m</sub>(°C) = 81.5 + 16.6(log<sub>10</sub>[Na<sup>+</sup>]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na<sup>+</sup>] is the concentration of sodium ions in the hybridization buffer ([Na<sup>+</sup>] for 1xSSC = 0.165 M).

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Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds.,

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John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

20

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

30

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell

strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include 5 *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by 10 phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, 15 and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an 20 insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or 25 cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using 30 such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin

(TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLabs (Beverly, MA), Pharmacia (Piscataway, NJ) and Invitrogen Corporation (Carlsbad, CA), respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such 5 epitope. One such epitope ("Flag") is commercially available from the Eastman Kodak Company (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or 10 all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic 15 animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are 20 known to those skilled in the art. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic 25 compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications 30 of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art

(see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are believed to be encompassed by the present invention.

### USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, those

described in Gyuris *et al.*, 1993, *Cell* 75: 791-803 and in Rossi *et al.*, 1997, *Proc. Natl. Acad. Sci. USA* 94: 8405-8410, all of which are incorporated by reference herein) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

5 The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which  
10 the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify  
15 inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

20 Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

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#### Nutritional Uses

30 Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors 5 discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, 10 MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. 15 Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro assays for Mouse Lymphocyte Function* 3.1-3.19; Chapter 7, *Immunologic studies in Humans*); Takai et al., *J. Immunol.* 137:3494-3500, 1986; Bertagnolli et al., *J. Immunol.* 145:1706-1712, 1990; Bertagnolli et al., *Cellular Immunology* 133:327-341, 1991; Bertagnolli, et al., *J. Immunol.* 149:3778-3783, 1992; Bowman et al., *J. 20 Immunol.* 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: *Polyclonal T cell stimulation*, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and 25 *Measurement of mouse and human Interferon  $\gamma$* , Schreiber, R.D. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: *Measurement of Human and Murine Interleukin 2 and Interleukin 4*, Bottomly, K., Davis, L.S. and Lipsky, P.E. In *Current 30 Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., *J. Exp. Med.* 173:1205-1211, 1991; Moreau et al., *Nature* 336:690-692, 1988; Greenberger et al., *Proc. Natl. Acad. Sci. U.S.A.* 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991;

Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: 10 *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 15 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or 20 immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune 25 deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, *Leishmania* spp., *malaria* spp. and various fungal infections 30 such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic

lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic 5 reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to regulate immune 10 responses in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, 15 process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the 20 absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, 25 blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, 30 monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this

matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated 5 administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in 10 humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science 257:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., 15 Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating 20 autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting 25 receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of 30 human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected *ex vivo* with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II

molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and  $\beta_2$  microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain 5 protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such 10 as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

15 The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates 20 and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 25 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

30 Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: *In vitro* antibody production, Mond, J.J. and Brunswick, M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

#### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines,

thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity)

5 useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of

10 hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or

15 *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

20 Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. *Cellular Biology* 15:141-151, 1995; Keller et al., *Molecular and Cellular Biology* 13:473-486, 1993; McClanahan et al., *Blood* 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., *Proc. Natl. Acad. Sci. USA* 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., *Experimental Hematology* 22:353-359,

1994; Cobblestone area forming cell assay, Ploemacher, R.E. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 163-179, 5 Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

10 A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

15 A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of 20 congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

25 A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

30 Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and

other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce 5 differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal 10 tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in 15 the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve 20 tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager 25 syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

30 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac)

and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

5 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

10 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

15 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium ).

20 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### Activin/Inhibin Activity

25 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts 30 of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for

advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

5 Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

10 Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell 15 population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

20 A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known 25 assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent 30 chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and

beta Chemokines 6.12.1-6.12.28; Taub et al. *J. Clin. Invest.* 95:1370-1376, 1995; Lind et al. *APMIS* 103:140-146, 1995; Muller et al *Eur. J. Immunol.* 25: 1744-1748; Gruber et al. *J. of Immunol.* 152:5860-5867, 1994; Johnston et al. *J. of Immunol.* 153: 1762-1768, 1994.

5        Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other 10 causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

15        The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., *J. Clin. Pharmacol.* 26:131-140, 1986; Burdick et al., *Thrombosis Res.* 45:413-419, 1987; Humphrey et al., *Fibrinolysis* 5:71-79 (1991); Schaub, *Prostaglandins* 35:467-474, 1988.

20

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their 25 ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also 30 useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: *Current Protocols in Immunology*, Ed by J.E. Coligan, A.M. Kruisbeek, D.H.

5 Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 10 1995.

#### Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in 15 the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat 20 inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting 25 from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### Cadherin/Tumor Invasion Suppressor Activity

Cadherins are calcium-dependent adhesion molecules that appear to play major 30 roles during development, particularly in defining specific cell types. Loss or alteration of normal cadherin expression can lead to changes in cell adhesion properties linked to tumor growth and metastasis. Cadherin malfunction is also implicated in other human diseases, such as pemphigus vulgaris and pemphigus foliaceus (auto-immune blistering skin diseases), Crohn's disease, and some developmental abnormalities.

The cadherin superfamily includes well over forty members, each with a distinct pattern of expression. All members of the superfamily have in common conserved extracellular repeats (cadherin domains), but structural differences are found in other parts of the molecule. The cadherin domains bind calcium to form their tertiary structure 5 and thus calcium is required to mediate their adhesion. Only a few amino acids in the first cadherin domain provide the basis for homophilic adhesion; modification of this recognition site can change the specificity of a cadherin so that instead of recognizing only itself, the mutant molecule can now also bind to a different cadherin. In addition, some cadherins engage in heterophilic adhesion with other cadherins.

10 E-cadherin, one member of the cadherin superfamily, is expressed in epithelial cell types. Pathologically, if E-cadherin expression is lost in a tumor, the malignant cells become invasive and the cancer metastasizes. Transfection of cancer cell lines with polynucleotides expressing E-cadherin has reversed cancer-associated changes by returning altered cell shapes to normal, restoring cells' adhesiveness to each other and to 15 their substrate, decreasing the cell growth rate, and drastically reducing anchorage-independent cell growth. Thus, reintroducing E-cadherin expression reverts carcinomas to a less advanced stage. It is likely that other cadherins have the same invasion suppressor role in carcinomas derived from other tissue types. Therefore, proteins of the present invention with cadherin activity, and polynucleotides of the present invention 20 encoding such proteins, can be used to treat cancer. Introducing such proteins or polynucleotides into cancer cells can reduce or eliminate the cancerous changes observed in these cells by providing normal cadherin expression.

Cancer cells have also been shown to express cadherins of a different tissue type than their origin, thus allowing these cells to invade and metastasize in a different tissue 25 in the body. Proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be substituted in these cells for the inappropriately expressed cadherins, restoring normal cell adhesive properties and reducing or eliminating the tendency of the cells to metastasize.

30 Additionally, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be used to generate antibodies recognizing and binding to cadherins. Such antibodies can be used to block the adhesion of inappropriately expressed tumor-cell cadherins, preventing the cells from forming a tumor elsewhere. Such an anti-cadherin antibody can also be used as a marker for the grade, pathological type, and prognosis of a cancer, i.e. the more progressed the

cancer, the less cadherin expression there will be, and this decrease in cadherin expression can be detected by the use of a cadherin-binding antibody.

Fragments of proteins of the present invention with cadherin activity, preferably a polypeptide comprising a decapeptide of the cadherin recognition site, and polynucleotides of the present invention encoding such protein fragments, can also be used to block cadherin function by binding to cadherins and preventing them from binding in ways that produce undesirable effects. Additionally, fragments of proteins of the present invention with cadherin activity, preferably truncated soluble cadherin fragments which have been found to be stable in the circulation of cancer patients, and polynucleotides encoding such protein fragments, can be used to disturb proper cell-cell adhesion.

Assays for cadherin adhesive and invasive suppressor activity include, without limitation, those described in: Hortsch et al. J Biol Chem 270 (32): 18809-18817, 1995; Miyaki et al. Oncogene 11: 2547-2552, 1995; Ozawa et al. Cell 63: 1033-1038, 1990.

#### 15 Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via antibody-dependent cell-mediated cytotoxicity (ADCC)). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

25

#### Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism,

anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and  
5 violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for  
10 example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### ADMINISTRATION AND DOSING

15 A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term  
20 "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11,  
25 IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention,  
30 or to minimize side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent.

A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

5 The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following 10 presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin 15 and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other 20 pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the 25 art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is 30 sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to

a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a 5 mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be 10 administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic 15 factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. 20 Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or 25 an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain 30 physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to 5 pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The 10 pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. 15 Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not 20 increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01  $\mu$ g to about 100 mg (preferably about 0.1ng to about 10 mg, more preferably about 0.1  $\mu$ g to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the 25 present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous 30 therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal and monoclonal antibodies which specifically react with the protein. As used herein, the term "antibody" includes without limitation a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a single-chain antibody, a CDR-grafted

antibody, a humanized antibody, or fragments thereof which bind to the indicated protein. Such term also includes any other species derived from an antibody or antibody sequence which is capable of binding the indicated protein.

Antibodies to a particular protein can be produced by methods well known to those skilled in the art. For example, monoclonal antibodies can be produced by generation of antibody-producing hybridomas in accordance with known methods (see for example, Goding, 1983, *Monoclonal antibodies: principles and practice*, Academic Press Inc., New York; and Yokoyama, 1992, "Production of Monoclonal Antibodies" in *Current Protocols in Immunology*, Unit 2.5, Greene Publishing Assoc. and John Wiley & Sons). Polyclonal sera and antibodies can be produced by inoculation of a mammalian subject with the relevant protein or fragments thereof in accordance with known methods. Fragments of antibodies, receptors, or other reactive peptides can be produced from the corresponding antibodies by cleavage of and collection of the desired fragments in accordance with known methods (see for example, Goding, *supra*; and Andrew et al., 1992, "Fragmentation of Immunoglobulins" in *Current Protocols in Immunology*, Unit 2.8, Greene Publishing Assoc. and John Wiley & Sons). Chimeric antibodies and single chain antibodies can also be produced in accordance with known recombinant methods (see for example, 5,169,939, 5,194,594, and 5,576,184). Humanized antibodies can also be made from corresponding murine antibodies in accordance with well known methods (see for example, U.S. Patent Nos. 5,530,101, 5,585,089, and 5,693,762). Additionally, human antibodies may be produced in non-human animals such as mice that have been genetically altered to express human antibody molecules (see for example Fishwild *et al.*, 1996, *Nature Biotechnology* **14**: 845-851; Mendez *et al.*, 1997, *Nature Genetics* **15**: 146-156 (erratum *Nature Genetics* **16**: 410); and U.S. Patents 5,877,397 and 5,625,126). Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, *J. Amer.Chem.Soc.* **85**, 2149-2154 (1963); J.L. Krstenansky, *et al.*, *FEBS Lett.* **211**, 10 (1987).

Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions

associated with the protein and also in the treatment of some forms of cancer where abnormal expression of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by 5 the protein.

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a 10 pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or 15 additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. 20 Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential 25 matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and 30 chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-

aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns.

5 In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, 10 ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 15 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

20 In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF).

25 The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering 30 various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in

the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline 5 labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without 10 limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

15 Patent and literature references cited herein are incorporated by reference as if fully set forth.

What is claimed is:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:1;
  - (b) the nucleotide sequence of SEQ ID NO:1 from nucleotide 126 to nucleotide 485;
  - (c) the nucleotide sequence of SEQ ID NO:1 from nucleotide 207 to nucleotide 485;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vb2\_1 deposited under accession number ATCC 98804;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
    - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2;
    - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
    - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:1.
2. The polynucleotide of claim 1 wherein said polynucleotide is operably linked to at least one expression control sequence.
3. A host cell transformed with the polynucleotide of claim 2.

4. The host cell of claim 3, wherein said cell is a mammalian cell.
5. A process for producing a protein encoded by the polynucleotide of claim 2, which process comprises:
  - (a) growing a culture of a host cell transformed with the polynucleotide of claim 2 in a suitable culture medium; and
  - (b) purifying said protein from the culture.
6. A protein produced according to the process of claim 5.
7. An isolated polynucleotide encoding the protein of claim 6.
8. The polynucleotide of claim 7, wherein the polynucleotide comprises the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804.
9. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vb2\_1 deposited under accession number ATCC 98804;the protein being substantially free from other mammalian proteins.
10. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.
11. A composition comprising the protein of claim 9 and a pharmaceutically acceptable carrier.
12. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:3;

- (b) the nucleotide sequence of SEQ ID NO:3 from nucleotide 130 to nucleotide 2286;
- (c) the nucleotide sequence of SEQ ID NO:3 from nucleotide 214 to nucleotide 2286;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb3\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb3\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:4;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:3.

13. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:4;
- (b) a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb3\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

14. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:5;
- (b) the nucleotide sequence of SEQ ID NO:5 from nucleotide 172 to nucleotide 522;
- (c) the nucleotide sequence of SEQ ID NO:5 from nucleotide 214 to nucleotide 522;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb4\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:6;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising eight contiguous amino acids of SEQ ID NO:6;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:5.

15. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:6;
- (b) a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising eight contiguous amino acids of SEQ ID NO:6; and

(c) the amino acid sequence encoded by the cDNA insert of clone vb4\_1 deposited under accession number ATCC 98804; the protein being substantially free from other mammalian proteins.

16. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:7;
- (b) the nucleotide sequence of SEQ ID NO:7 from nucleotide 119 to nucleotide 502;
- (c) the nucleotide sequence of SEQ ID NO:7 from nucleotide 176 to nucleotide 502;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb5\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:8;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:7.

17. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:8;
- (b) a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb5\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

18. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:9;
- (b) the nucleotide sequence of SEQ ID NO:9 from nucleotide 128 to nucleotide 436;
- (c) the nucleotide sequence of SEQ ID NO:9 from nucleotide 203 to nucleotide 436;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb6\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:10;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:9.

19. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:10;
- (b) a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb6\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

20. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:11;
- (b) the nucleotide sequence of SEQ ID NO:11 from nucleotide 138 to nucleotide 1250;
- (c) the nucleotide sequence of SEQ ID NO:11 from nucleotide 279 to nucleotide 1250;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb7\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:12;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:11.

21. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:12;
- (b) a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb7\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

22. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:13;
- (b) the nucleotide sequence of SEQ ID NO:13 from nucleotide 615 to nucleotide 869;
- (c) the nucleotide sequence of the full-length protein coding sequence of clone vb8\_1 deposited under accession number ATCC 98804;
- (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:14;
- (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14;
- (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
- (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:13.

23. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:14;
- (b) a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb8\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

24. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:15;
- (b) the nucleotide sequence of SEQ ID NO:15 from nucleotide 148 to nucleotide 1470;
- (c) the nucleotide sequence of SEQ ID NO:15 from nucleotide 193 to nucleotide 1470;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb9\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:16;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:15.

25. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:16;
- (b) a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb9\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

26. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:17;
- (b) the nucleotide sequence of SEQ ID NO:17 from nucleotide 109 to nucleotide 414;
- (c) the nucleotide sequence of SEQ ID NO:17 from nucleotide 217 to nucleotide 414;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc3\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:18;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18, the fragment comprising eight contiguous amino acids of SEQ ID NO:18;

- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:17.

27. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:18;
- (b) a fragment of the amino acid sequence of SEQ ID NO:18, the fragment comprising eight contiguous amino acids of SEQ ID NO:18; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc3\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

28. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:19;
- (b) the nucleotide sequence of SEQ ID NO:19 from nucleotide 169 to nucleotide 840;
- (c) the nucleotide sequence of SEQ ID NO:19 from nucleotide 211 to nucleotide 840;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc4\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:20;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:19.

29. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:20;
- (b) a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc4\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

30. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:21;
- (b) the nucleotide sequence of SEQ ID NO:21 from nucleotide 508 to nucleotide 951;
- (c) the nucleotide sequence of SEQ ID NO:21 from nucleotide 733 to nucleotide 951;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc5\_1 deposited under accession number ATCC 98748;

- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:22;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:21.

31. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:22;
- (b) a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc5\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

32. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:23;
- (b) the nucleotide sequence of SEQ ID NO:23 from nucleotide 125 to nucleotide 493;
- (c) the nucleotide sequence of the full-length protein coding sequence of clone vc7\_1 deposited under accession number ATCC 98748;
- (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;

- (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:24;
- (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24;
- (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
- (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:23.

33. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:24;
- (b) a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc7\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

34. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:25;
- (b) the nucleotide sequence of SEQ ID NO:25 from nucleotide 33 to nucleotide 407;
- (c) the nucleotide sequence of SEQ ID NO:25 from nucleotide 99 to nucleotide 407;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc9\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;

- (f) the nucleotide sequence of a mature protein coding sequence of clone vc9\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:26;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:25.

35. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:26;
- (b) a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc9\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

36. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:27;
- (b) the nucleotide sequence of SEQ ID NO:27 from nucleotide 176 to nucleotide 871;
- (c) the nucleotide sequence of the full-length protein coding sequence of clone vc10\_1 deposited under accession number ATCC 98748;

- (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:28;
- (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28;
- (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
- (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:27.

37. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:28;
- (b) a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc10\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

38. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:29;
- (b) the nucleotide sequence of SEQ ID NO:29 from nucleotide 160 to nucleotide 657;
- (c) the nucleotide sequence of SEQ ID NO:29 from nucleotide 214 to nucleotide 657;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc11\_1 deposited under accession number ATCC 98748;

- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc11\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:30;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30, the fragment comprising eight contiguous amino acids of SEQ ID NO:30;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:29.

39. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:30;
- (b) a fragment of the amino acid sequence of SEQ ID NO:30, the fragment comprising eight contiguous amino acids of SEQ ID NO:30; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc11\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

40. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:31;
- (b) the nucleotide sequence of SEQ ID NO:31 from nucleotide 228 to nucleotide 662;

- (c) the nucleotide sequence of SEQ ID NO:31 from nucleotide 327 to nucleotide 662;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc14\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc14\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:32;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:31.

41. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:32;
- (b) a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc14\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

42. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:33;
- (b) the nucleotide sequence of SEQ ID NO:33 from nucleotide 101 to nucleotide 667;
- (c) the nucleotide sequence of SEQ ID NO:33 from nucleotide 182 to nucleotide 667;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc16\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:34;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:33.

43. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:34;
- (b) a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc16\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

44. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:35;
- (b) the nucleotide sequence of SEQ ID NO:35 from nucleotide 8 to nucleotide 355;
- (c) the nucleotide sequence of SEQ ID NO:35 from nucleotide 134 to nucleotide 355;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc17\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc17\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:36;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:35.

45. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:36;
- (b) a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc17\_1 deposited under accession number ATCC 98784; the protein being substantially free from other mammalian proteins.

46. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:37;
- (b) the nucleotide sequence of SEQ ID NO:37 from nucleotide 1031 to nucleotide 1252;
- (c) the nucleotide sequence of SEQ ID NO:37 from nucleotide 1100 to nucleotide 1252;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc21\_1 deposited under accession number ATCC 98785;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:38;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:37.

47. A protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:38;  
(b) the amino acid sequence of SEQ ID NO:38 from amino acid 29 to amino acid 74;  
(c) a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38; and  
(d) the amino acid sequence encoded by the cDNA insert of clone vc21\_1 deposited under accession number ATCC 98785;  
the protein being substantially free from other mammalian proteins.

48. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:39;
- (b) the nucleotide sequence of SEQ ID NO:39 from nucleotide 94 to nucleotide 1482;
- (c) the nucleotide sequence of SEQ ID NO:39 from nucleotide 214 to nucleotide 1482;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc23\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc23\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:40;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:39.

49. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:40;
- (b) a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc23\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

50. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:41;
- (b) the nucleotide sequence of SEQ ID NO:41 from nucleotide 153 to nucleotide 413;
- (c) the nucleotide sequence of SEQ ID NO:41 from nucleotide 264 to nucleotide 413;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc25\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:42;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42;

- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:41.

51. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:42;
- (b) a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc25\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

52. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:43;
- (b) the nucleotide sequence of SEQ ID NO:43 from nucleotide 87 to nucleotide 1409;
- (c) the nucleotide sequence of SEQ ID NO:43 from nucleotide 156 to nucleotide 1409;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc26\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:44;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:43.

53. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:44;
- (b) a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc26\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

54. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:45;
- (b) the nucleotide sequence of SEQ ID NO:45 from nucleotide 63 to nucleotide 428;
- (c) the nucleotide sequence of SEQ ID NO:45 from nucleotide 156 to nucleotide 428;
- (d) the nucleotide sequence of SEQ ID NO:45 from nucleotide 356 to nucleotide 1773;
- (e) the nucleotide sequence of the full-length protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804;
- (f) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

- (g) the nucleotide sequence of a mature protein coding sequence of clone vc30\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;
- (i) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:46;
- (j) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46;
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h); and
- (l) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h), and that has a length that is at least 25% of the length of SEQ ID NO:45.

55. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:46;
- (b) the amino acid sequence of SEQ ID NO:46 from amino acid 1 to amino acid 97;
- (c) a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vc30\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

56. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:47;
- (b) the nucleotide sequence of SEQ ID NO:47 from nucleotide 30 to nucleotide 1799;

- (c) the nucleotide sequence of SEQ ID NO:47 from nucleotide 90 to nucleotide 1799;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vd1\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:48;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:47.

57. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:48;
- (b) a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vd1\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

58. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:49;
- (b) the nucleotide sequence of SEQ ID NO:49 from nucleotide 69 to nucleotide 443;
- (c) the nucleotide sequence of SEQ ID NO:49 from nucleotide 111 to nucleotide 443;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vd2\_1 deposited under accession number ATCC 98748;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:50;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:49.

59. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:50;
- (b) a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vd2\_1 deposited under accession number ATCC 98748;

the protein being substantially free from other mammalian proteins.

60. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:51;
- (b) the nucleotide sequence of SEQ ID NO:51 from nucleotide 176 to nucleotide 1249;
- (c) the nucleotide sequence of SEQ ID NO:51 from nucleotide 227 to nucleotide 1249;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vd3\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:52;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:51.

61. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:52;
- (b) a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52; and

(c) the amino acid sequence encoded by the cDNA insert of clone vd3\_1 deposited under accession number ATCC 98804;  
the protein being substantially free from other mammalian proteins.

62. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:53;
- (b) the nucleotide sequence of SEQ ID NO:53 from nucleotide 94 to nucleotide 1530;
- (c) the nucleotide sequence of SEQ ID NO:53 from nucleotide 145 to nucleotide 1530;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vd4\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:54;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:53.

63. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:54;
- (b) a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vd4\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

64. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:55;
- (b) the nucleotide sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1300;
- (c) the nucleotide sequence of SEQ ID NO:55 from nucleotide 182 to nucleotide 1300;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone ve4\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:56;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:55.

65. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:56;
- (b) a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve4\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

66. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:57;
- (b) the nucleotide sequence of SEQ ID NO:57 from nucleotide 57 to nucleotide 785;
- (c) the nucleotide sequence of SEQ ID NO:57 from nucleotide 147 to nucleotide 785;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone ve8\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:58;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:57.

67. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:58;
- (b) a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve8\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

68. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:59;
- (b) the nucleotide sequence of SEQ ID NO:59 from nucleotide 64 to nucleotide 1002;
- (c) the nucleotide sequence of SEQ ID NO:59 from nucleotide 139 to nucleotide 1002;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vf1\_1 deposited under accession number ATCC 98784;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vf1\_1 deposited under accession number ATCC 98784;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:60;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60;

- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:59.

69. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:60;
- (b) a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf1\_1 deposited under accession number ATCC 98784;

the protein being substantially free from other mammalian proteins.

70. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:61;
- (b) the nucleotide sequence of SEQ ID NO:61 from nucleotide 588 to nucleotide 995;
- (c) the nucleotide sequence of SEQ ID NO:61 from nucleotide 750 to nucleotide 995;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vh1\_1 deposited under accession number ATCC 98804;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:62;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:61.

71. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:62;
- (b) a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vh1\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

72. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:63;
- (b) the nucleotide sequence of SEQ ID NO:63 from nucleotide 29 to nucleotide 1369;
- (c) the nucleotide sequence of SEQ ID NO:63 from nucleotide 104 to nucleotide 1369;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vi1\_1 deposited under accession number ATCC 98804;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vi1\_1 deposited under accession number ATCC 98804;

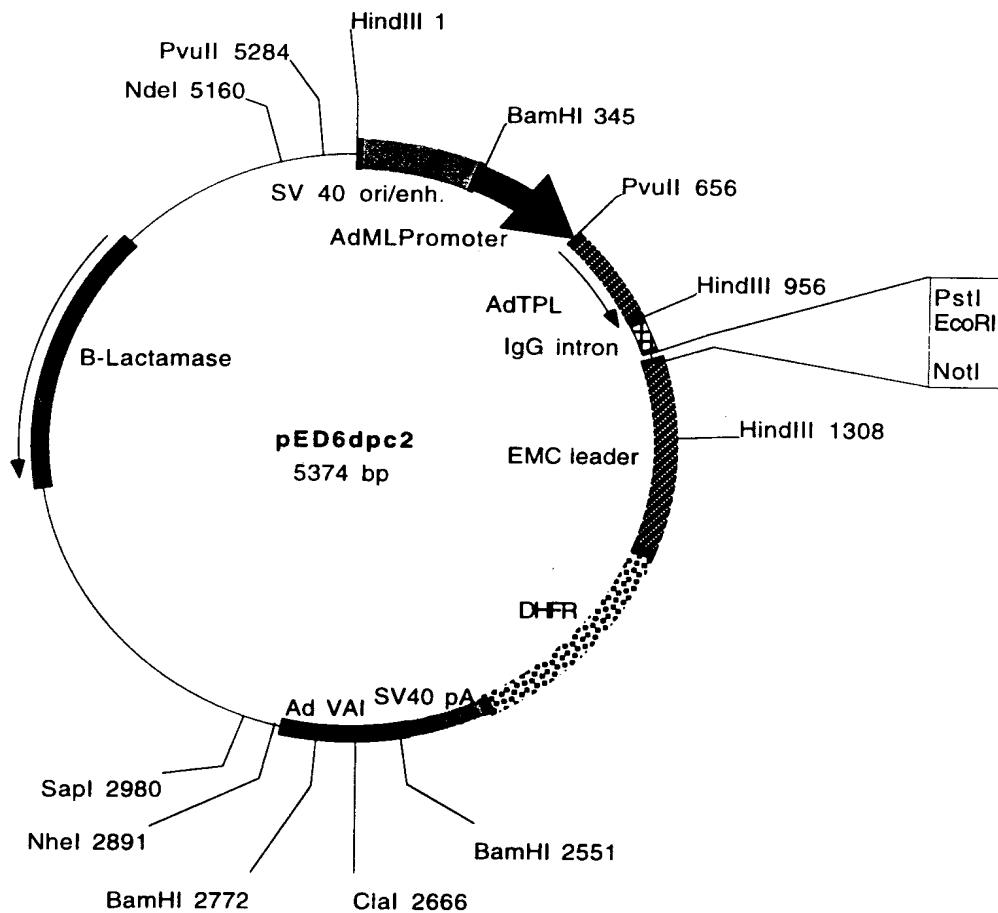
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:64;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:63.

73. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:64;
- (b) a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vi1\_1 deposited under accession number ATCC 98804;

the protein being substantially free from other mammalian proteins.

FIGURE 1A

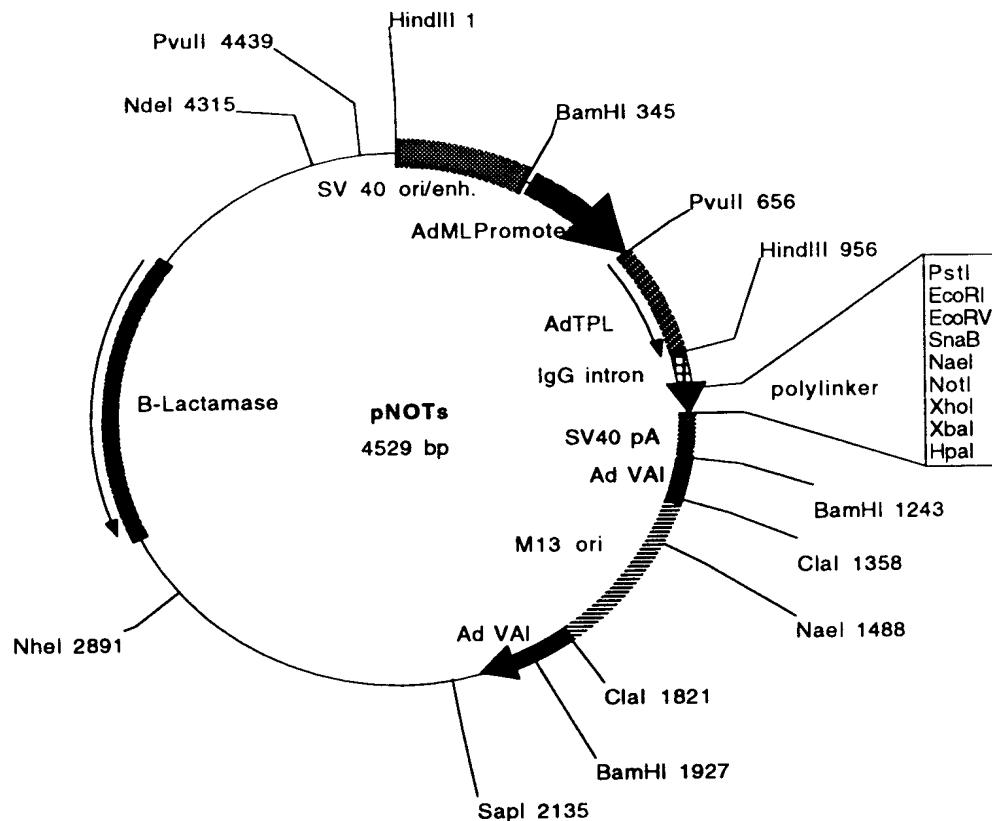


**Plasmid name:** pED6dpc2

**Plasmid size:** 5374 bp

**Comments/References:** pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SST cDNAs are cloned between EcoRI and NotI. pED vectors are described in Kaufman et al.(1991), NAR 19: 4485-4490.

FIGURE 1B



**Plasmid name:** pNOTs

**Plasmid size:** 4529 bp

**Comments/References:** pNOTs is a derivative of pMT2 (Kaufman et al, 1989. Mol. Cell. Biol. 9:1741-1750). DHFR was deleted and a new polylinker was inserted between EcoRI and HpaI. M13 origin of replication was inserted in the Clal site. SST cDNAs are cloned between EcoRI and NotI.

## SEQUENCE LISTING

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Yuan, Olive  
Hoffman, Heidi  
Hall, Jeff  
Rapiejko, Peter  
AlphaGene, Inc.

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<210> 10  
 <211> 103  
 <212> PRT  
 <213> Homo sapiens

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Thr Pro Leu His Ser Leu Ser Trp Ser Leu Ile Ser Met Ser Ser Arg  
 20 25 30

Arg Val Lys Lys Gly Thr Lys Ser Arg Ser Phe Lys Pro His Pro His  
 35 40 45

Leu Arg Met Asp Gly Phe Leu Cys Arg Pro Cys Arg Pro Leu Ser Gln  
 50 55 60

Gln	Thr	Phe	Pro	Ala	Ala	Leu	Glu	Pro	Ser	Lys	Thr	Ser	Thr	Thr	Ser
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70															
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Leu	Ile	Arg	Pro	Ser	Trp	Leu									
	100														

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<211> 1760  
<212> DNA  
<213> Homo sapiens

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<210> 12  
<211> 371  
<212> PRT  
<213> Homo sapiens

<400> 12  
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Pro Met Glu Glu Asp Gly Leu Arg Trp Thr Pro Lys Ser Pro Leu Asp  
20 25 30

Pro Asp Ser Gly Leu Leu Ser Cys Thr Leu Pro Asn Gly Phe Gly Gly

35

40

45

Gln Ser Gly Pro Glu Gly Glu Arg Ser Leu Ala Pro Pro Asp Ala Ser  
 50 55 60

Ile Leu Ile Ser Asn Val Cys Ser Ile Gly Asp His Val Ala Gln Glu  
 65 70 75 80

Leu Phe Gln Gly Ser Asp Leu Gly Met Ala Glu Glu Ala Glu Arg Pro  
 85 90 95

Gly Glu Lys Ala Gly Gln His Ser Pro Leu Arg Glu Glu His Val Thr  
 100 105 110

Cys Val Gln Ser Ile Leu Asp Glu Phe Leu Gln Thr Tyr Gly Ser Leu  
 115 120 125

Ile Pro Leu Ser Thr Asp Glu Val Val Glu Lys Leu Glu Asp Ile Phe  
 130 135 140

Gln Gln Glu Phe Ser Thr Pro Ser Arg Lys Gly Leu Val Leu Gln Leu  
 145 150 155 160

Ile Gln Ser Tyr Gln Arg Met Pro Gly Asn Ala Met Val Arg Gly Phe  
 165 170 175

Arg Val Ala Tyr Lys Arg His Val Leu Thr Met Asp Asp Leu Gly Thr  
 180 185 190

Leu Tyr Gly Gln Asn Trp Leu Asn Asp Gln Val Met Asn Met Tyr Gly  
 195 200 205

Asp Leu Val Met Asp Thr Val Pro Glu Lys Val His Phe Phe Asn Ser  
 210 215 220

Phe Phe Tyr Asp Lys Leu Arg Thr Lys Gly Tyr Asp Gly Val Lys Arg  
 225 230 235 240

Trp Thr Lys Asn Val Asp Ile Phe Asn Lys Glu Leu Leu Ile Pro  
 245 250 255

Ile His Leu Glu Val His Trp Ser Leu Ile Ser Val Asp Val Arg Arg  
 260 265 270

Arg Thr Ile Thr Tyr Phe Asp Ser Gln Arg Thr Leu Asn Arg Arg Cys  
 275 280 285

Pro Lys His Ile Ala Lys Tyr Leu Gln Ala Glu Ala Val Lys Lys Asp  
 290 295 300

Arg Leu Asp Phe His Gln Gly Trp Lys Gly Tyr Phe Lys Met Asn Val  
 305 310 315 320

Ala Arg Gln Asn Asn Asp Ser Asp Cys Gly Ala Phe Val Leu Gln Tyr  
 325 330 335

Cys Lys His Leu Ala Leu Ser Gln Pro Phe Ser Phe Thr Gln Gln Asp  
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Met Pro Lys Leu Arg Arg Gln Ile Tyr Lys Glu Leu Cys His Cys Lys

355

360

365

Leu Thr Val  
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<210> 13  
<211> 1299  
<212> DNA  
<213> Homo sapiens

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<210> 14  
<211> 85  
<212> PRT  
<213> Homo sapiens

<400> 14  
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Pro Gly Met Ser Lys Leu Cys Cys Ser Gly Ala Ser Cys His Leu Leu  
20 25 30  
Gly Leu Ile Pro His Leu Ile Pro Tyr Arg Glu Lys Cys Glu Phe Arg  
35 40 45  
Trp Arg Val Gly Pro Gly Pro Met Arg His Gln Trp Lys His Ser Ser  
50 55 60  
Lys Phe Arg Gln Val Pro Leu Glu Arg Lys Thr Met Thr Gly Lys Cys  
65 70 75 80  
Ile Ser Ser Gly Val  
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<210> 15  
 <211> 2996  
 <212> DNA  
 <213> Homo sapiens

<400> 15  
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<210> 16  
 <211> 441  
 <212> PRT

<213> Homo sapiens

<400> 16

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20			25			30										
Gln Gln His Gly Tyr Pro Glu Pro Gly Ala Gly Ser Pro Gly Ser Gly																
35			40			45										
Tyr Ala Ser Arg Arg His Trp Cys His His Thr Val Thr Arg Thr Val																
50			55			60										
Ser Cys Gln Val Gln Asn Gly Ser Glu Thr Val Val Gln Arg Val Tyr																
65			70			75									80	
Gln Ser Cys Arg Trp Pro Gly Pro Cys Ala Asn Leu Val Ser Tyr Arg																
85			90			95										
Thr Leu Ile Arg Pro Thr Tyr Arg Val Ser Tyr Arg Thr Val Thr Val																
100			105			110										
Leu Glu Trp Arg Cys Cys Pro Gly Phe Thr Gly Ser Asn Cys Asp Glu																
115			120			125										
Glu Cys Met Asn Cys Thr Arg Leu Ser Asp Met Ser Glu Arg Leu Thr																
130			135			140										
Thr Leu Glu Ala Lys Val Leu Leu Leu Glu Ala Ala Glu Arg Pro Ser																
145			150			155									160	
Ser Pro Asp Asn Asp Leu Pro Ala Pro Glu Ser Thr Pro Pro Thr Trp																
165			170			175										
Asn Glu Asp Phe Leu Pro Asp Ala Ile Pro Leu Ala His Pro Val Pro																
180			185			190										
Arg Gln Arg Arg Pro Thr Gly Pro Ala Gly Pro Pro Gly Gln Thr Gly																
195			200			205										
Pro Pro Gly Pro Ala Gly Pro Pro Gly Ser Lys Gly Asp Arg Gly Gln																
210			215			220										
Thr Gly Glu Lys Gly Pro Ala Gly Pro Pro Gly Leu Leu Gly Pro Pro																
225			230			235									240	
Gly Pro Arg Gly Leu Pro Gly Glu Met Gly Arg Pro Gly Pro Pro Gly																
245			250			255										
Pro Pro Gly Pro Ala Gly Asn Pro Gly Pro Ser Pro Asn Ser Pro Gln																
260			265			270										
Gly Ala Leu Tyr Ser Leu Gln Pro Pro Thr Asp Lys Asp Asn Gly Asp																
275			280			285										
Ser Arg Leu Ala Ser Ala Ile Val Asp Thr Val Leu Ala Gly Val Pro																
290			295			300										

Gly Pro Arg Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Pro Arg Gly  
 305 310 315 320  
 Pro Pro Gly Pro Pro Gly Thr Pro Gly Ser Gln Gly Leu Ala Gly Glu  
 325 330 335  
 Arg Gly Thr Val Gly Pro Ser Gly Glu Pro Gly Val Lys Gly Glu Glu  
 340 345 350  
 Gly Glu Lys Ala Ala Thr Ala Glu Gly Glu Val Gln Gln Leu Arg  
 355 360 365  
 Glu Ala Leu Lys Ile Leu Ala Glu Arg Val Leu Ile Leu Glu His Met  
 370 375 380  
 Ile Gly Ile His Asp Pro Leu Ala Ser Pro Glu Gly Gly Ser Gly Gln  
 385 390 395 400  
 Asp Ala Ala Leu Arg Ala Asn Leu Lys Met Lys Arg Gly Gly Ala Gln  
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 Pro Asp Gly Val Leu Ala Ala Leu Leu Gly Pro Asp Pro Gly Gln Lys  
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 Ser Val Asp Gln Ala Ser Ser Arg Lys  
 435 440

<210> 17  
 <211> 850  
 <212> DNA  
 <213> Homo sapiens

<400> 17  
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 aaaaaaaaaaa 850

<210> 18  
 <211> 102  
 <212> PRT  
 <213> Homo sapiens

<400> 18  
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 1 5 10 15

Met Val Gly Tyr Val Leu Gly Pro Phe Phe Leu Ile Thr Leu Val Gly

20

25

30

Val	Val	Val	Ala	Val	Val	Met	Tyr	Val	Gln	Lys	Lys	Lys	Arg	Val	Asp
35						40							45		
Arg	Leu	Arg	His	His	Leu	Leu	Pro	Met	Tyr	Ser	Tyr	Asp	Pro	Ala	Glu
50						55							60		
Glu	Leu	His	Glu	Ala	Glu	Gln	Glu	Leu	Leu	Ser	Asp	Met	Gly	Asp	Pro
65						70							75		80
Lys	Val	Val	His	Gly	Trp	Gln	Ser	Gly	Tyr	Gln	His	Lys	Arg	Met	Pro
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Leu	Leu	Asp	Val	Lys	Thr										
					100										

&lt;210&gt; 19

&lt;211&gt; 1108

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

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&lt;210&gt; 20

&lt;211&gt; 224

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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Pro	Asp	Thr	Phe	Asp	Asp	Thr	Tyr	Val	Gly	Cys	Ala	Glu	Glu	Met	Glu
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Glu	Lys	Ala	Ala	Pro	Leu	Leu	Lys	Glu	Glu	Met	Ala	His	His	Ala	Leu
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Ile Met Val Tyr Thr Asn Ser Ser Asn Thr Leu Tyr Trp Glu Leu Asn		
100	105	110
Gln Ala Val Arg Thr Gly Gly Ser Arg Glu Leu Tyr Met Arg His		
115	120	125
Phe Pro Phe Lys Ala Leu His Phe Tyr Leu Ile Arg Ala Leu Gln Leu		
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Leu Arg Gly Ser Gly Gly Cys Ser Arg Gly Pro Gly Glu Val Val Phe		
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Arg Gly Val Gly Ser Leu Arg Phe Glu Pro Lys Arg Leu Gly Asp Ser		
165	170	175
Val Arg Leu Gly Gln Phe Ala Ser Ser Ser Leu Asp Lys Ala Val Ala		
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His Arg Phe Gly Glu Lys Arg Arg Gly Cys Val Ser Ala Pro Gly Ala		
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<212> DNA
<213> Homo sapiens
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 <213> Homo sapiens

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Arg Arg Glu Arg Gly Val Ser Pro Arg Pro Gly Ala Gly Lys Glu Cys  
 35 40 45

Val Ala Gln Leu Ser Ala Leu Leu Ile Leu Ile Met Glu Lys Pro Leu  
 50 55 60

Phe Leu Ser Pro Phe Pro Glu Leu Val Phe Cys Cys Phe Cys Phe Ile  
 65 70 75 80

Leu Phe Trp Gly Asp Ser Phe Leu Leu Phe Asn Leu Glu Ser Pro Val  
 85 90 95

Pro Leu Gly Cys Arg Gln Phe Leu Pro Gly Pro Ser Arg Asn Pro His  
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Ser Pro Ser Pro Leu Leu Arg Tyr Leu Gln Glu Ala Ala Asn Leu Val  
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&lt;210&gt; 24

&lt;211&gt; 123

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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									20				25		30

His	Leu	Leu	His	Gly	Tyr	Ile	Lys	Leu	Leu	Thr	Val	Ser	Thr	Leu	Ser
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Cys	Tyr	Leu	Gln	Asn	Trp	Asp	Asn	Met	Ile	Pro	Ser	Val	Ala	Ile	Val
								50				55		60	

Phe	Leu	Ile	Trp	Pro	Arg	Asp	Leu	Leu	Lys	Leu	Asp	Met	Gly	Gly	Asn
									65			70		75	80

Leu	Phe	Cys	Phe	Gly	Ile	Gln	Lys	Gly	Asn	Ile	Cys	Lys	Thr	Val	Leu
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Lys	Asp	Gln	Lys	Ser	Cys	Ser	Tyr	Phe	Asp	Cys	Tyr	Asn	Leu	Leu	Ile
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<211> 4466

<212> DNA

<213> Homo sapiens

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&lt;210&gt; 26

&lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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					20				25				30		

Gly	Leu	Ala	Gln	Cys	Ile	Gln	Leu	Pro	Thr	Gly	Leu	Val	Gln	Arg	Gln
					35			40				45			

Pro	Cys	Leu	Pro	Glu	His	Gly	Ile	Phe	Lys	Asn	Pro	Pro	Ala	Leu	Gly
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Ser	Val	Cys	Ser	His	Pro	Gly	Ser	Ile	Arg	Ser	Leu	Leu	Cys	Arg	Arg
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&lt;210&gt; 27

&lt;211&gt; 2667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

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&lt;210&gt; 28

&lt;211&gt; 232

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

Met	Ser	Arg	Thr	Arg	Glu	Gly	Pro	Arg	Arg	Trp	Trp	Thr	Gly	Pro	Val
1	5						10					15			

Ala Arg Gly Ala Leu Gly Trp Gly Leu Cys Met Cys Leu Lys Val Ala

20

25

30

Ala Val Arg His Ser Phe Ser Pro Pro Pro His Pro Thr Gly Arg Ala  
 35 40 45

Ala Arg Arg Pro Cys Gly Ser Asp Ser Arg Trp Cys Pro Trp Pro Pro  
 50 55 60

Cys Gly Ser Pro Ala Cys Cys Gly Ser Thr Cys Pro Ala Ser Gly Ser  
 65 70 75 80

Thr Ser Ser Thr Pro Ser Gln Ser Gln Ala Pro Ser Pro Thr Arg Pro  
 85 90 95

Ser Ser Ala Pro Thr Glu Val Arg Arg Pro Leu Trp Trp Glu Ser Arg  
 100 105 110

Val Gly Ser Trp Ala Glu Pro Gln Leu Arg Ser Leu Tyr Leu Leu Pro  
 115 120 125

Arg His Pro Ala Pro Gln Ile Pro Leu His Arg Arg Pro Gly Gly His  
 130 135 140

Pro Ala Pro Glu Arg Leu Gly Ala Pro Val Gln Gln Ile Arg Gly Trp  
 145 150 155 160

Pro Arg Arg Glu Pro Pro Val Arg Val Leu His Leu Pro Gly Gly Asp  
 165 170 175

Arg Gly Thr Gly Gln Ala Gln Glu Asp Arg Asp Arg His Leu His Gln  
 180 185 190

Val Glu Gln Gly Leu Pro Gly Arg Gly Val Ala Gly Arg His Leu Leu  
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His Gln His Ala Val Val Pro Gly Val Gly Gly Val Arg Gln Gly Glu  
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Gly Gln Arg Ala Pro Arg Ala His  
 225 230

<210> 29

<211> 2699

<212> DNA

<213> Homo sapiens

<400> 29

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&lt;210&gt; 30

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

Met	Gly	Phe	Ile	Pro	Leu	Pro	Leu	Ala	Val	Leu	Leu	Ile	Arg	Val	Val
1															
				5					10					15	

Thr	Ser	Ser	Ile	Lys	Val	Gln	Gly	Ile	Leu	Ser	Tyr	Ala	Cys	Val	Ile
									20					30	

Leu	Phe	Tyr	Phe	Gly	Leu	Ile	Ser	Leu	Lys	Val	Leu	Asn	Ser	Ile	Val
									35					45	

Leu	Leu	Gly	Lys	Ser	Cys	Gln	Tyr	Val	Lys	Glu	Ala	Lys	Met	Glu	Glu
									50					60	

Lys	Leu	Ser	Asn	Pro	Pro	Ala	Thr	Cys	Thr	Pro	Gly	Lys	Pro	Ser	Ser
									65					80	

Lys	Ser	Gln	Asn	Lys	Cys	Lys	Pro	Ser	Gln	Gly	Leu	Ser	Thr	Glu	Glu
									85					95	

Asn	Leu	Ser	Ala	Ser	Ile	Thr	Lys	Gln	Pro	Ile	His	Gln	Lys	Glu	Asn
									100					110	

Ile Ile Pro Leu Leu Val Thr Ser Asn Ser Asp Gln Phe Leu Thr Thr  
 115 120 125

Pro Asp Gly Asp Glu Lys Asp Ile Thr Gln Asp Asn Ser Glu Leu Lys  
 130 135 140

His Arg Ser Ser Lys Lys Asp Leu Leu Glu Ile Asp Arg Phe Thr Ile  
 145 150 155 160

Cys Gly Asn Arg Ile Asp  
 165

<210> 31

<211> 1300

<212> DNA

<213> Homo sapiens

<400> 31

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<210> 32

<211> 145

<212> PRT

<213> Homo sapiens

<400> 32

Met Ile Pro Ile Trp Lys Gln Gln Ala Arg Pro Gly Asp Gly Pro Val  
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Ile Trp Asp Tyr His Val Val Leu Leu His Val Ser Ser Gly Gly Gln  
 20 25 30

Ser Phe Ile Tyr Asp Leu Asp Thr Val Leu Pro Phe Pro Cys Leu Phe  
 35 40 45

Asp Thr Tyr Val Glu Asp Ala Ile Lys Ser Asp Asp Asp Ile His Pro  
 50 55 60

Gln Phe Arg Arg Lys Phe Arg Val Ile Cys Ala Asp Ser Tyr Leu Lys  
 65 70 75 80

Asn Phe Ala Ser Asp Arg Ser His Met Lys Asp Ser Ser Gly Asn Trp  
 85 90 95

Arg Glu Pro Pro Pro Tyr Pro Cys Ile Glu Thr Gly Asp Ser Lys  
 100 105 110

Met Asn Leu Asn Asp Phe Ile Ser Met Asp Pro Lys Val Gly Trp Gly  
 115 120 125

Ala Val Tyr Thr Leu Ser Glu Phe Thr His Arg Phe Gly Ser Lys Asn  
 130 135 140

Cys

145

<210> 33

<211> 1256

<212> DNA

<213> Homo sapiens

<400> 33

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<210> 34

<211> 189

<212> PRT

<213> Homo sapiens

<400> 34

Met Thr Leu Ala Ala Tyr Lys Glu Lys Met Lys Glu Leu Pro Leu Val  
 1 5 10 15

Ser Leu Phe Cys Ser Cys Phe Leu Ala Asp Pro Leu Asn Lys Ser Ser  
 20 25 30

Tyr	Lys	Tyr	Glu	Ala	Asp	Thr	Val	Asp	Leu	Asn	Trp	Cys	Val	Ile	Ser
35							40						45		
Asp	Met	Glu	Val	Ile	Glu	Leu	Asn	Lys	Cys	Thr	Ser	Gly	Gln	Ser	Phe
50							55						60		
Glu	Val	Ile	Leu	Lys	Pro	Pro	Ser	Phe	Asp	Gly	Val	Pro	Glu	Phe	Asn
65							70						75		80
Ala	Ser	Leu	Pro	Arg	Arg	Arg	Asp	Pro	Ser	Leu	Glu	Glu	Ile	Gln	Lys
							85						90		95
Lys	Leu	Glu	Ala	Ala	Glu	Glu	Arg	Arg	Lys	Tyr	Gln	Glu	Ala	Glu	Leu
							100						105		110
Leu	Lys	His	Leu	Ala	Glu	Lys	Arg	Glu	His	Glu	Arg	Glu	Val	Ile	Gln
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Lys	Ala	Ile	Glu	Glu	Asn	Asn	Asn	Phe	Ile	Lys	Met	Ala	Lys	Glu	Lys
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Leu	Ala	Gln	Lys	Met	Glu	Ser	Asn	Lys	Glu	Asn	Arg	Glu	Ala	His	Leu
													145		160
Ala	Ala	Met	Leu	Glu	Arg	Leu	Gln	Glu	Lys	Asp	Lys	His	Ala	Glu	Glu
													165		175
Val	Arg	Lys	Asn	Lys	Glu	Leu	Lys	Glu	Glu	Glu	Ala	Ser	Arg		
													180		185

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<210> 36  
 <211> 116  
 <212> PRT  
 <213> Homo sapiens

<400> 36  
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 20 25 30  
 Ser Val Ala Leu Pro Ser Leu Leu Ala Ser Glu Ser Phe Asp Ser  
 35 40 45  
 Ile Tyr Pro Gly Ile Phe Cys Val Leu Met Phe Ser Ser Gly Leu Val  
 50 55 60  
 Ser Ala Val Leu Ile Gly Arg Ala Leu Ser Phe Gln Ala Ile Leu Lys  
 65 70 75 80  
 Gly Gly Gln Ser Lys Gly Gln Ser Leu Asn Pro Phe Cys Gly Leu Asn  
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<210> 37  
 <211> 1725  
 <212> DNA  
 <213> Homo sapiens

<400> 37  
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&lt;210&gt; 38

&lt;211&gt; 74

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 38

Met	Ile	Trp	Gly	Ala	Met	Lys	Gly	Ala	Met	Gln	Glu	Leu	Leu	Leu	Pro
1															15

Ser	Ser	Leu	Val	Thr	Trp	Gly	Cys	Gln	Ala	Gly	Phe	Trp	Lys	Thr	Ser
															20
															25
															30

Ala	Leu	Lys	Leu	Ile	Leu	Lys	Arg	Ala	Val	Pro	Ala	Leu	Trp	Pro	Pro
															35
															40
															45

Gly	Gly	Pro	Asp	Ser	Pro	Glu	Thr	Thr	Phe	Cys	Pro	Lys	Asn	Met	Leu
															50
															55
															60

Ser	Ile	Trp	Gly	Ile	Ser	Ser	His	Lys	Pro
									65
									70

&lt;210&gt; 39

&lt;211&gt; 1953

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

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 ctttgcattt ttggaggtca ttggccagc agtcaagaaa ctatggaaa gtcaccattt 240  
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 ataaagatcc acactttaa taagacattt acacaagaag agaaaatcaa gcaatagat 480  
 gcacttgaat ttctgtccatt tgaaggaaaaa gtgaatttta agaaaaccgca acatgtattt 540  
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&lt;210&gt; 40

&lt;211&gt; 463

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

Met Ala Leu Ser Cys Thr Leu Asn Arg Tyr Leu Leu Leu Met Ala Gln

1 5 10 15

Glu His Leu Glu Phe Arg Leu Pro Glu Ile Lys Ser Leu Leu Leu  
20 25 30Phe Gly Gly Gln Phe Ala Ser Ser Gln Glu Thr Tyr Gly Lys Ser Pro  
35 40 45Phe Trp Ile Leu Ser Ile Pro Ser Glu Asp Ile Ala Arg Asn Leu Met  
50 55 60Lys Arg Thr Val Cys Ala Lys Ser Ile Phe Glu Leu Trp Gly His Gly  
65 70 75 80Gln Ser Pro Glu Glu Leu Tyr Ser Ser Leu Lys Asn Tyr Pro Val Glu  
85 90 95Lys Met Val Pro Phe Leu His Ser Asp Ser Thr Tyr Lys Ile Lys Ile  
100 105 110His Thr Phe Asn Lys Thr Leu Thr Gln Glu Glu Lys Ile Lys Arg Ile  
115 120 125Asp Ala Leu Glu Phe Leu Pro Phe Glu Gly Lys Val Asn Leu Lys Lys  
130 135 140Pro Gln His Val Phe Ser Val Leu Glu Asp Tyr Gly Leu Asp Pro Asn  
145 150 155 160Cys Ile Pro Glu Asn Pro His Asn Ile Tyr Phe Gly Arg Trp Ile Ala  
165 170 175Asp Gly Gln Arg Glu Leu Ile Glu Ser Tyr Ser Val Lys Lys Arg His  
180 185 190

Phe Ile Gly Asn Thr Ser Met Asp Ala Gly Leu Ser Phe Ile Met Ala

195	200	205
Asn His Gly Lys Val Lys Glu Asn Asp Ile Val Phe Asp Pro Phe Val		
210	215	220
Gly Thr Gly Gly Leu Leu Ile Ala Cys Ala His Phe Gly Ala Tyr Val		
225	230	235
Tyr Gly Thr Asp Ile Asp Tyr Asn Thr Val His Gly Leu Gly Lys Ala		
245	250	255
Thr Arg Lys Asn Gln Lys Trp Arg Gly Pro Asp Glu Asn Ile Arg Ala		
260	265	270
Asn Leu Arg Gln Tyr Gly Leu Glu Lys Tyr Tyr Leu Asp Val Leu Val		
275	280	285
Ser Asp Ala Ser Lys Pro Ser Trp Arg Lys Gly Thr Tyr Phe Asp Ala		
290	295	300
Ile Ile Thr Asp Pro Pro Tyr Gly Ile Arg Glu Ser Thr Arg Arg Thr		
305	310	315
Gly Ser Gln Lys Glu Ile Pro Lys Gly Ile Glu Lys Trp Glu Lys Cys		
325	330	335
Pro Glu Ser His Val Pro Val Ser Leu Ser Tyr His Leu Ser Asp Met		
340	345	350
Phe Leu Asp Leu Leu Asn Phe Ala Ala Glu Thr Leu Val Leu Gly Gly		
355	360	365
Arg Leu Val Tyr Trp Leu Pro Val Tyr Thr Pro Glu Tyr Thr Glu Glu		
370	375	380
Met Val Pro Trp His Pro Cys Leu Glu Leu Val Ser Asn Cys Glu Gln		
385	390	395
Lys Leu Ser Ser His Thr Ser Arg Arg Leu Ile Thr Met Glu Lys Val		
405	410	415
Lys Lys Phe Glu Asn Arg Asp Gln Tyr Ser His Leu Leu Ser Asp His		
420	425	430
Phe Leu Pro Tyr Gln Gly His Asn Ser Phe Arg Glu Lys Tyr Phe Ser		
435	440	445
Gly Val Thr Lys Arg Ile Ala Lys Glu Glu Lys Ser Thr Gln Glu		
450	455	460
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<211> 1605		
<212> DNA		
<213> Homo sapiens		
<400> 41		
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&lt;210&gt; 42

&lt;211&gt; 87

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

Met	Glu	Trp	His	Ser	Val	Leu	Met	Asp	Phe	His	Phe	Phe	Ala	Leu	Leu
1					5				10					15	

Arg	Arg	Gln	Ser	Gln	Pro	Leu	Arg	Ser	Leu	Pro	His	Leu	Cys	His	Leu
						20			25				30		

Pro	Gly	Ser	Cys	Ser	Leu	Met	Tyr	Leu	Trp	Val	Val	Arg	Trp	Lys	Trp
						35			40			45			

Cys	Leu	Gln	Lys	Leu	Gly	Arg	Arg	Ile	Leu	Leu	His	Ser	Leu	His	Asp
						50			55			60			

Val	Phe	Ile	Ala	Asn	Met	Asp	Asp	Lys	Gly	Leu	Cys	Tyr	Arg	Gly	Leu
						65			70			75		80	

Arg	Ala	Pro	Ser	Phe	Leu	Leu
				85		

&lt;210&gt; 43

&lt;211&gt; 1936

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 43

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 aaaaaaaaaa aaaaaaa 1936

<210> 44  
 <211> 441  
 <212> PRT  
 <213> Homo sapiens

<400> 44

Met Ala Ile His Lys Ala Leu Val Met Cys Leu Gly Leu Pro Leu Phe  
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Leu Phe Pro Gly Ala Trp Ala Gln Gly His Val Pro Pro Gly Cys Ser  
 20 25 30

Gln Gly Leu Asn Pro Leu Tyr Tyr Asn Leu Cys Asp Arg Ser Gly Ala  
 35 40 45

Trp Gly Ile Val Leu Glu Ala Val Ala Gly Ile Val Thr Thr  
 50 55 60

Phe Val Leu Thr Ile Ile Leu Val Ala Ser Leu Pro Phe Val Gln Asp  
 65 70 75 80

Thr Lys Lys Arg Ser Leu Leu Gly Thr Gln Val Phe Phe Leu Leu Gly  
 85 90 95

Thr Leu Gly Leu Phe Cys Leu Val Phe Ala Cys Val Val Lys Pro Asp  
 100 105 110

Phe Ser Thr Cys Ala Ser Arg Arg Phe Leu Phe Gly Val Leu Phe Ala  
 115 120 125

Ile Cys Phe Ser Cys Leu Ala Ala His Val Phe Ala Leu Asn Phe Leu  
 130 135 140  
 Ala Arg Lys Asn His Gly Pro Arg Gly Trp Val Ile Phe Thr Val Ala  
 145 150 155 160  
 Leu Leu Leu Thr Leu Val Glu Val Ile Ile Asn Thr Glu Trp Leu Ile  
 165 170 175  
 Ile Thr Leu Val Arg Gly Ser Gly Glu Gly Pro Gln Gly Asn Ser  
 180 185 190  
 Ser Ala Gly Trp Ala Val Ala Ser Pro Cys Ala Ile Ala Asn Met Asp  
 195 200 205  
 Phe Val Met Ala Leu Ile Tyr Val Met Leu Leu Leu Leu Gly Ala Phe  
 210 215 220  
 Leu Gly Ala Trp Pro Ala Leu Cys Gly Arg Tyr Lys Arg Trp Arg Lys  
 225 230 235 240  
 His Gly Val Phe Val Leu Leu Thr Thr Ala Thr Ser Val Ala Ile Trp  
 245 250 255  
 Val Val Trp Ile Val Met Tyr Thr Tyr Gly Asn Lys Gln His Asn Ser  
 260 265 270  
 Pro Thr Trp Asp Asp Pro Thr Leu Ala Ile Ala Leu Ala Ala Asn Ala  
 275 280 285  
 Trp Ala Phe Val Leu Phe Tyr Val Ile Pro Glu Val Ser Gln Val Thr  
 290 295 300  
 Lys Ser Ser Pro Glu Gln Ser Tyr Gln Gly Asp Met Tyr Pro Thr Arg  
 305 310 315 320  
 Gly Val Gly Tyr Glu Thr Ile Leu Lys Glu Gln Lys Gly Gln Ser Met  
 325 330 335  
 Phe Val Glu Asn Lys Ala Phe Ser Met Asp Glu Pro Val Ala Ala Lys  
 340 345 350  
 Arg Pro Val Ser Pro Tyr Ser Gly Tyr Asn Gly Gln Leu Leu Thr Ser  
 355 360 365  
 Val Tyr Gln Pro Thr Glu Met Ala Leu Met His Lys Val Pro Ser Glu  
 370 375 380  
 Gly Ala Tyr Asp Ile Ile Leu Pro Arg Ala Thr Ala Asn Ser Gln Val  
 385 390 395 400  
 Met Gly Ser Ala Asn Ser Thr Leu Arg Ala Glu Asp Met Tyr Ser Ala  
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 Gln Ser His Gln Ala Ala Thr Pro Pro Lys Asp Gly Lys Asn Ser Gln  
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 Val Phe Arg Asn Pro Tyr Val Trp Asp  
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<210> 45  
 <211> 1773  
 <212> DNA  
 <213> Homo sapiens

<400> 45  
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<210> 46  
 <211> 122  
 <212> PRT  
 <213> Homo sapiens

<400> 46  
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 Val Arg Val Ala Glu Tyr Arg Asn His Trp Ser Asp Val Leu Ala Gly  
 35 40 45  
 Phe Leu Thr Gly Ala Ala Ile Ala Thr Phe Leu Val Thr Cys Val Val  
 50 55 60  
 His Asn Phe Gln Ser Arg Pro Pro Ser Gly Arg Arg Leu Ser Pro Trp  
 65 70 75 80  
 Glu Asp Leu Gly Gln Ala Pro Thr Met Asp Ser Pro Leu Glu Lys Asn

85

90

95

Pro Arg Ser Ala Gly Arg Ile Arg His Arg His Gly Ser Pro His Pro  
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Ser Arg Arg Thr Ala Pro Ala Val Ala Thr  
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<210> 47  
<211> 1974  
<212> DNA  
<213> *Homo sapien*

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cctggaggggg ttgggggtgg gggacagggtt tctgaaatcc ctgaagggggg ttgtactggg 1920  
atttgtgaat aaacttgata cactatgttgc tcaaaaaaaaaaaaaaaa aaaa 1974

<210> 48  
<211> 590  
<212> PRT  
<213> *Homo sapiens*

<400> 48  
Met His Leu Ala Arg Leu Val Gly Ser Cys Ser Leu Leu Leu Leu Leu  
1 5 10 15

Gly Ala Leu Ser Gly Trp Ala Ala Ser Asp Asp Pro Ile Glu Lys Val  
20 25 30

Ile Glu Gly Ile Asn Arg Gly Leu Ser Asn Ala Glu Arg Glu Val Gly  
35 40 45

Lys Ala Leu Asp Gly Ile Asn Ser Gly Ile Thr His Ala Gly Arg Glu  
50 55 60

Val Glu Lys Val Phe Asn Gly Leu Ser Asn Met Gly Ser His Thr Gly  
65 70 75 80

Lys Glu Leu Asp Lys Gly Val Gln Gly Leu Asn His Gly Met Asp Lys  
85 90 95

Val Ala His Glu Ile Asn His Gly Ile Gly Gln Ala Gly Lys Glu Ala  
100 105 110

Glu Lys Leu Gly His Gly Val Asn Asn Ala Ala Gly Gln Val Gly Lys  
115 120 125

Glu Ala Asp Lys Leu Ile His His Gly Val His His Gly Ala Asn Gln  
130 135 140

Ala Gly Ser Glu Ala Gly Lys Phe Gly Gln Gly Val Asp Asn Ala Ala  
145 150 155 160

Gly Gln Ala Gly Asn Glu Ala Gly Arg Phe Gly Gln Gly Val His His  
165 170 175

Ala Ala Gly Gln Ala Gly Asn Glu Ala Gly Arg Phe Gly Gln Gly Val  
180 185 190

His His Ala Ala Gly Gln Ala Gly Asn Glu Ala Gly Arg Phe Gly Gln  
195 200 205

Gly Ala His His Gly Leu Ser Glu Gly Trp Lys Glu Thr Glu Lys Phe  
210 215 220

Gly Gln Gly Ile His His Ala Ala Gly Gln Val Gly Lys Glu Ala Glu  
225 230 235 240

Lys Phe Gly Gln Gly Ala His His Ala Ala Gly Gln Ala Gly Asn Glu  
245 250 255

Ala Gly Arg Phe Gly Gln Gly Val His His Gly Leu Ser Glu Gly Trp  
260 265 270

Lys Glu Thr Glu Lys Phe Gly Gln Gly Val His His Thr Ala Gly Gln  
275 280 285

Val Gly Lys Glu Ala Glu Lys Phe Gly Gln Gly Ala His His Ala Ala  
290 295 300

Gly Gln Ala Gly Asn Glu Ala Gly Arg Phe Gly Gln Gly Ala His His  
305 310 315 320

Ala Ala Gly Gln Ala Gly Asn Glu Ala Gly Arg Phe Gly Gln Gly Val  
325 330 335

His His Gly Leu Ser Glu Gly Trp Lys Glu Thr Glu Lys Phe Gly Gln  
340 345 350

Gly Val His His Ala Ala Ser Gln Phe Gly Lys Glu Thr Glu Lys Leu  
 355 360 365  
 Gly His Gly Val His His Gly Val Asn Glu Ala Trp Lys Glu Ala Glu  
 370 375 380  
 Lys Phe Gly Gln Gly Val His His Ala Ala Ser Gln Val Gly Lys Glu  
 385 390 395 400  
 Glu Asp Arg Val Val Gln Gly Leu His His Gly Val Ser Gln Ala Gly  
 405 410 415  
 Arg Glu Gly Gly Gln Phe Gly His Asp Ile His His Thr Ala Gly Gln  
 420 425 430  
 Ala Gly Lys Glu Gly Asp Ile Ala Val His Gly Val Gln Pro Gly Val  
 435 440 445  
 His Glu Ala Gly Lys Glu Ala Gly Gln Phe Gly Gln Gly Val His His  
 450 455 460  
 Thr Leu Glu Gln Ala Gly Lys Glu Ala Asp Lys Ala Val Gln Gly Phe  
 465 470 475 480  
 His Thr Gly Val His Gln Ala Gly Lys Glu Ala Glu Lys Leu Gly Gln  
 485 490 495  
 Gly Val Asn His Ala Ala Asp Gln Ala Gly Lys Glu Val Glu Lys Leu  
 500 505 510  
 Gly Gln Gly Ala His His Ala Ala Gly Gln Ala Gly Lys Glu Leu Gln  
 515 520 525  
 Asn Ala His Asn Gly Val Asn Gln Ala Ser Lys Glu Ala Asn Gln Leu  
 530 535 540  
 Leu Asn Gly Asn His Gln Ser Gly Ser Ser Ser His Gln Gly Gly Ala  
 545 550 555 560  
 Thr Thr Thr Pro Leu Ala Ser Gly Ala Ser Val Asn Thr Pro Phe Ile  
 565 570 575  
 Asn Leu Pro Ala Leu Trp Arg Ser Val Ala Asn Ile Met Pro  
 580 585 590

<210> 49  
 <211> 923  
 <212> DNA  
 <213> Homo sapiens

<400> 49  
 gagagctgga tccttgaaaa tctactctat cagctgctgt gggtgccacc attctcagga 60  
 ccctcgccat gaaaagccctt atgctgctca ccctgtctgt tctgctctgc tgggtctcag 120  
 ctgacattcg ctgtcactcc tgctacaagg tccctgtgt gggctgtgtg gaccggcagt 180  
 cctgcccgcct ggagccagga cagcaatgcc tgacaacaca tgcataccctt ggtaagatgt 240  
 gggttttctc caatctgcgc tgtggcacac cagaagagcc ctgtcaggag gccttcaacc 300  
 aaacccaaccc taagctgggt ctgacatata acaccacctg ctgcaacaag gacaactgca 360  
 acagcgcagg accccggccc actccagccc tgggccttgc ctcccttacc tccttgctg 420

gccttggcct ctggctgctg cactgagact cattccattg gctgcccctc ctcccacctg 480  
 ccttggcctg agcctcttc cctgtgtctc tgtatcccct ggctttacag aatcgctct 540  
 ccctagctcc catttcttta attaaacact gttccgagtg gtctcctcat ccgtccttcc 600  
 cacctcacac ctttcaactct ctttttctg ggtcccttcc cacttccttc caggacctcc 660  
 attggctctt agaagggctc cccactttgc ttccataact ctgctgtccc ctacttgagg 720  
 agggattggg atctggggcc taaaaatgggg cttctgtgtt gtccccagtg aaggctccca 780  
 caaggacctg atgacacctac tgtacagagc tgactccca aatccaggct cccatatgt 840  
 ccccatcccc catactcacc tctttccatt ttgagtaata aatgtctgag tctgaaaaaa 900  
 aaaaaaaaaa aaaaaaaaaa aaa 923

&lt;210&gt; 50

&lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

Met	Lys	Ala	Leu	Met	Leu	Leu	Thr	Leu	Ser	Val	Leu	Leu	Cys	Trp	Val
1															

Ser	Ala	Asp	Ile	Arg	Cys	His	Ser	Cys	Tyr	Lys	Val	Pro	Val	Leu	Gly
							20		25						30

Cys	Val	Asp	Arg	Gln	Ser	Cys	Arg	Leu	Glu	Pro	Gly	Gln	Gln	Cys	Leu
							35		40						45

Thr	Thr	His	Ala	Tyr	Leu	Gly	Lys	Met	Trp	Val	Phe	Ser	Asn	Leu	Arg
							50		55						60

Cys	Gly	Thr	Pro	Glu	Glu	Pro	Cys	Gln	Glu	Ala	Phe	Asn	Gln	Thr	Asn
							65		70						80

Arg	Lys	Leu	Gly	Leu	Thr	Tyr	Asn	Thr	Thr	Cys	Cys	Asn	Lys	Asp	Asn
							85		90						95

Cys	Asn	Ser	Ala	Gly	Pro	Arg	Pro	Thr	Pro	Ala	Leu	Gly	Leu	Val	Phe
							100		105						110

Leu	Thr	Ser	Leu	Ala	Gly	Leu	Gly	Leu	Trp	Leu	Leu	His			
							115		120						125

&lt;210&gt; 51

&lt;211&gt; 1493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 51

ggagaagccc aggcaaggta ggacaggaga gagaaggctg cagacccaga gggagggagg 60  
 acaggaggatc ggaaggagga ggacagagga gggcacagag acgcagagca agggcgccaa 120  
 ggaggagacc ctgggtggag gaagacactc tggagagaga gggggctggg cagagatgaa 180  
 gttccaggggg cccctggct gcctcctgt gcctcctgtc ctgggcagtg gggaggctgg 240  
 cccctgcag agcggagagg aaagcactgg gacaatatt ggggaggccc ttggacatgg 300  
 cctgggagac gcccctgagcg aagggttggg aaaggccatt ggcaaaagagg ccggaggggc 360  
 agctggctct aaagtcaagtgg agggcccttgg ccaaggacc agagaaggcag ttggcactgg 420  
 agtcaggcag gttcaggct ttggcgttagc agatgtttg ggcaacaggc tcggggaaagc 480  
 agcccattgt ctggaaacaca ctgggcacga gattggcaga caggcagaag atgtcattcg 540  
 acacggagca gatgtgtcc gcggctccgt gcagggggtg cctggccaca atggtgcctg 600  
 ggaaaactct ggaggccatg gcatctttgg ctctcaagggt ggcccttggag gcccaggccaa 660  
 gggcaatctt ggaggtctgg ggactccgtg ggtccacgga taccgggaa actcagcagg 720  
 cagctttgga atgaatcctc agggagctcc ctggggtaaa ggaggcaatg gaggccacc 780

aaactttggg accaacactc agggagctgt ggcccagcct ggctatggtt cagttagagc 840  
 cagcaaccag aatgaagggt gcacgaatcc cccaccatct ggctcaggtg gaggctccag 900  
 caactctggg ggagggcagcg gctcacagtc gggcagcagt ggcagtgca gcaatggta 960  
 caacaacaat ggcagcagca gtggtggca cagcagtggc agcagcagtgc gcccagcag 1020  
 tggcggcagc agtggtggca gcagtgca cagtggc agcagaggtg acagcggcag 1080  
 tgagtccccc tggggatcca gcaccggctc ctcctccggc aaccacggc gaggcggcga 1140  
 gggaaatggac ataaacccgg gaactctgag acgtctcctg ggatgtttaa ctttgacact 1200  
 ttcttggaga attttaatc caagctgggt ttcatcaact gggatgccc aaacaaggac 1260  
 cagagaagct ctcgcatccc gtgacctcca gacaaggagc caccagattg gatgggagcc 1320  
 cccacactcc ctccttaaaa caccaccctc tcatcaactaa tctcagccct tgcccttgaa 1380  
 ataaaaccta gctgccccac aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 1493

<210> 52

<211> 358

<212> PRT

<213> Homo sapiens

<400> 52

Met Lys Phe Gln Gly Pro Leu Ala Cys Leu Leu Leu Ala Leu Cys Leu  
 1 5 10 15

Gly Ser Gly Glu Ala Gly Pro Leu Gln Ser Gly Glu Ser Thr Gly  
 20 25 30

Thr Asn Ile Gly Glu Ala Leu Gly His Gly Leu Gly Asp Ala Leu Ser  
 35 40 45

Glu Gly Val Gly Lys Ala Ile Gly Lys Glu Ala Gly Gly Ala Ala Gly  
 50 55 60

Ser Lys Val Ser Glu Ala Leu Gly Gln Gly Thr Arg Glu Ala Val Gly  
 65 70 75 80

Thr Gly Val Arg Gln Val Pro Gly Phe Gly Val Ala Asp Ala Leu Gly  
 85 90 95

Asn Arg Val Gly Glu Ala Ala His Ala Leu Gly Asn Thr Gly His Glu  
 100 105 110

Ile Gly Arg Gln Ala Glu Asp Val Ile Arg His Gly Ala Asp Ala Val  
 115 120 125

Arg Gly Ser Trp Gln Gly Val Pro Gly His Asn Gly Ala Trp Glu Thr  
 130 135 140

Ser Gly Gly His Gly Ile Phe Gly Ser Gln Gly Gly Leu Gly Gly Gln  
 145 150 155 160

Gly Gln Gly Asn Pro Gly Gly Leu Gly Thr Pro Trp Val His Gly Tyr  
 165 170 175

Pro Gly Asn Ser Ala Gly Ser Phe Gly Met Asn Pro Gln Gly Ala Pro  
 180 185 190

Trp Gly Gln Gly Gly Asn Gly Gly Pro Pro Asn Phe Gly Thr Asn Thr  
 195 200 205

Gln Gly Ala Val Ala Gln Pro Gly Tyr Gly Ser Val Arg Ala Ser Asn  
 210 215 220

Gln Asn Glu Gly Cys Thr Asn Pro Pro Pro Ser Gly Ser Gly Gly  
 225 230 235 240  
 Ser Ser Asn Ser Gly Gly Ser Gly Ser Gln Ser Gly Ser Ser Gly  
 245 250 255  
 Ser Gly Ser Asn Gly Asp Asn Asn Asn Gly Ser Ser Ser Gly Gly Ser  
 260 265 270  
 Ser Ser Gly Ser Ser Ser Gly Gly Ser Ser Gly Gly Ser Ser Gly Gly  
 275 280 285  
 Ser Ser Gly Asn Ser Gly Gly Ser Arg Gly Asp Ser Gly Ser Glu Ser  
 290 295 300  
 Ser Trp Gly Ser Ser Thr Gly Ser Ser Ser Gly Asn His Gly Gly Ala  
 305 310 315 320  
 Ala Glu Glu Met Asp Ile Asn Pro Gly Thr Leu Arg Arg Leu Leu Gly  
 325 330 335  
 Cys Leu Thr Leu Thr Leu Ser Gly Arg Ile Leu Asn Pro Ser Trp Val  
 340 345 350  
 Ser Ser Thr Gly Met Pro  
 355

<210> 53  
 <211> 1897  
 <212> DNA  
 <213> Homo sapiens

<400> 53  
 acagaggagg gcacagagac gcagagcaag ggcggcaagg aggagaccc ggtgggagga 60  
 agacactctg gagagagagg gggctggca gagatgaagt tccaggggc cctggcctgc 120  
 ctcctgctgg ccctctgcct gggcagtggg gaggctggc ccctgcagag cggagagggaa 180  
 agcaactggga caaatattgg ggagggccctt ggacatggcc tgggagacgc cctgagccaa 240  
 ggggtgggaa aggccattgg caaagaggcc ggagggccag ctggctctaa agtcagttag 300  
 gccccttggcc aaggaccag agaagcagg tgcactggag tcaggcagg tccaggctt 360  
 ggcgtagcag atgctttggg caacagggtc ggggaagcag cccatgtct gggaaacact 420  
 gggcacgaga ttggcagaca ggcagaagat gtcatcgac acggagcaga tgctgtccgc 480  
 ggctcctggc aggggtgccc tggccacaat ggtgcttggg aaacttctgg aggcattggc 540  
 atctttggct ctcaaggtgg ctttggaggg cagggccagg gcaatcctgg aggtctgggg 600  
 actccgtggg tccacggata ccccgaaaac tcagcaggca gtttggaaat gaatcctcag 660  
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 ggagctgtgg cccagcctgg ctatggttca gtgagagcca gcaaccagaa tgaagggtgc 780  
 acgaatcccc caccatctgg ctcaggtgg ggctccagca actctggggg aggcagccgc 840  
 tcacagtctgg gcagcagtgg cagtggcagc aatggtgcaca acaacaatgg cagcagcagt 900  
 ggtggcagca gcagtggcag cagcagtggc ggcagcagt gggcagcagc tggcagc 960  
 agtggcaaca gtggcagcag cagaggtgac agcggcagtg agtcctcctg gggatccagc 1020  
 accggctctt cttccggcaaa ccacgggtgg agcggcggag gaaatggaca taaaccggg 1080  
 gggcaagggt cgagctgggg cagtggagga ggtgacgctg ttgtggaggt caatactgtg 1140  
 aactctgaga cgtctcctgg gatgttaac tttgacactt tctggaaagaa ttttaatcc 1200  
 aagctgggtt tcatcaactg ggtgccata aacaagaacc aggtccgc ccccagcacc 1260  
 cgagccctcc tctacttcag ccgactctgg gaggattca aacagaacac tcctttcctc 1320  
 aactggaaag caattattga gggcggcagc gcgtcatcac tgcagaaaacg tgcaggcaga 1380  
 gcccgtcaga actacaatta caaccagcat gcgtatccca ctgcctatgg tggaaagtac 1440  
 tcagtcaaga cccctgcaaa ggggggagtc tcaccttctt cctcggcttc ccgggtgcaa 1500

cctggcctgc tgcagtgggt gaagtttgg taggcaattt cttgcaacca ccaccgaggc 1560  
 cccgaaaagc actggtcgtc agggagctcc tccccttggc ccccagcctg tgccagccct 1620  
 gggcccggtc ccacacccctt gtttcctagg ctggggaccc agcttgcgtc tccttggttc 1680  
 ttcccactgc actgtgggtc ttcaagtggcc accagcctcg tcacatacac cagcatctt 1740  
 ctgtaccc tccctttggt gacctaagt cacttgaca gttctccagg aaggaggagc 1800  
 ttcctacttt tgagtttctc tgtggaaata aaacatgaat cttgtttccc taaaaaaaaa 1860  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1897

<210> 54  
 <211> 479  
 <212> PRT  
 <213> Homo sapiens

<400> 54  
 Met Lys Phe Gln Gly Pro Leu Ala Cys Leu Leu Leu Ala Leu Cys Leu  
 1 5 10 15  
 Gly Ser Gly Glu Ala Gly Pro Leu Gln Ser Gly Glu Glu Ser Thr Gly  
 20 25 30  
 Thr Asn Ile Gly Glu Ala Leu Gly His Gly Leu Gly Asp Ala Leu Ser  
 35 40 45  
 Glu Gly Val Gly Lys Ala Ile Gly Lys Glu Ala Gly Gly Ala Ala Gly  
 50 55 60  
 Ser Lys Val Ser Glu Ala Leu Gly Gln Gly Thr Arg Glu Ala Val Gly  
 65 70 75 80  
 Thr Gly Val Arg Gln Val Pro Gly Phe Gly Val Ala Asp Ala Leu Gly  
 85 90 95  
 Asn Arg Val Gly Glu Ala Ala His Ala Leu Gly Asn Thr Gly His Glu  
 100 105 110  
 Ile Gly Arg Gln Ala Glu Asp Val Ile Arg His Gly Ala Asp Ala Val  
 115 120 125  
 Arg Gly Ser Trp Gln Gly Val Pro Gly His Asn Gly Ala Trp Glu Thr  
 130 135 140  
 Ser Gly Gly His Gly Ile Phe Gly Ser Gln Gly Gly Leu Gly Gly Gln  
 145 150 155 160  
 Gly Gln Gly Asn Pro Gly Gly Leu Gly Thr Pro Trp Val His Gly Tyr  
 165 170 175  
 Pro Gly Asn Ser Ala Gly Ser Phe Gly Met Asn Pro Gln Gly Ala Pro  
 180 185 190  
 Trp Gly Gln Gly Gly Asn Gly Gly Pro Pro Asn Phe Gly Thr Asn Thr  
 195 200 205  
 Gln Gly Ala Val Ala Gln Pro Gly Tyr Gly Ser Val Arg Ala Ser Asn  
 210 215 220  
 Gln Asn Glu Gly Cys Thr Asn Pro Pro Pro Ser Gly Ser Gly Gly  
 225 230 235 240  
 Ser Ser Asn Ser Gly Gly Ser Gly Ser Gln Ser Gly Ser Ser Gly

245	250	255
Ser Gly Ser Asn Gly Asp Asn Asn Asn Gly Ser Ser Ser Gly Gly Ser		
260	265	270
Ser Ser Gly Ser Ser Ser Gly Gly Ser Ser Gly Gly Ser Ser Gly Gly		
275	280	285
Ser Ser Gly Asn Ser Gly Gly Ser Arg Gly Asp Ser Gly Ser Glu Ser		
290	295	300
Ser Trp Gly Ser Ser Thr Gly Ser Ser Ser Gly Asn His Gly Gly Ser		
305	310	315
Gly Gly Gly Asn Gly His Lys Pro Gly Gly Gln Gly Ser Ser Trp Gly		
325	330	335
Ser Gly Gly Asp Ala Val Gly Gly Val Asn Thr Val Asn Ser Glu		
340	345	350
Thr Ser Pro Gly Met Phe Asn Phe Asp Thr Phe Trp Lys Asn Phe Lys		
355	360	365
Ser Lys Leu Gly Phe Ile Asn Trp Asp Ala Ile Asn Lys Asn Gln Val		
370	375	380
Pro Pro Pro Ser Thr Arg Ala Leu Leu Tyr Phe Ser Arg Leu Trp Glu		
385	390	395
Asp Phe Lys Gln Asn Thr Pro Phe Leu Asn Trp Lys Ala Ile Ile Glu		
405	410	415
Gly Ala Asp Ala Ser Ser Leu Gln Lys Arg Ala Gly Arg Ala Asp Gln		
420	425	430
Asn Tyr Asn Tyr Asn Gln His Ala Tyr Pro Thr Ala Tyr Gly Lys		
435	440	445
Tyr Ser Val Lys Thr Pro Ala Lys Gly Val Ser Pro Ser Ser Ser		
450	455	460
Ala Ser Arg Val Gln Pro Gly Leu Leu Gln Trp Val Lys Phe Trp		
465	470	475

<210> 55  
 <211> 1532  
 <212> DNA  
 <213> Homo sapiens

<400> 55  
 gaagagcccc tgcggccggg cgcggaaatg gcggccggcg cgacggccgg gcgctcctga 60  
 agcagcagtt atggagcttc cctcagggcc gggccggag cgctctttt actcgacaccg 120  
 gcttccgggt gactgcttcc tactgctcgt gctgctgctc tacgcgccag tcgggttctg 180  
 cctcctcgtc ctgcgcctgt ttctcgggat ccacgtcttc ctggtcagct ggcgcgtgcc 240  
 agacagcgtc cttcgcagat tcgttagtgcg gaccatgtgt gccgtgctag ggctcggtgc 300  
 cccgcaggag gactccggac tccgggatca cagtgtcagg gtcctcattt ccaaccatgt 360  
 gacacctttc gaccacaaca tagtcaattt gcttaccacc ttagtgcaccc ctctactcaa 420  
 tagtcccccc agctttgtgt gctggtctcg gggcttcatg gagatgaatg ggccggggga 480  
 gttggtggag tcactcaaga gattctgtgc ttccacgagg cttcccccca ctcctctgct 540

gctattccct gaggaagagg ccaccaatgg ccgggagggg ctccctgcgt tcagttcctg 600  
 gccatttct atccaaagatg tggtaacaacc tcttaccctg caagttcaga gacccttggt 660  
 ctctgtacgt gtgtcagatg ctcctgggt ctcagaactg ctgtggtcac tttcgtccc 720  
 tttcacggtg tatcaagtaa ggtggcttcg tcctgttcat cgccaactag gggaaaggc 780  
 tgaggagttt gcactccgtg tacaacagct ggtggccaag gaattgggccc agacaggac 840  
 acggctcaact ccagctgaca aagcagagca catgaagcga caaagacacc ccagattgcg 900  
 cccccagtcg gcccagtctt cttccctcc ctccctgggt ccttctctg atgtgcaact 960  
 ggcaactctg gtcagagag tcaaggaagt tttgccttcat gtgcattgg gtgtcatcca 1020  
 gagagacctg gccaagactg gctgtgtaga cttgactatc actaatctgc ttgaggggc 1080  
 cgtagcttca atgcctgaag acatcaccaa gggaaactcag tccctaccca cagcctctgc 1140  
 ctccaaagttt cccagctctg gcccgggtgac ccctcagcca acagccctaa catttgccaa 1200  
 gtcttcctgg gcccggcagg agagcctgca ggagcgcag caagcactat atgaatacgc 1260  
 aagaaggaga ttcacagaga gacgagccca ggaggtgac ttagctcaaa ggaacaggat 1320  
 ggcacccaga gccgcaggac ggagactggg ggcagccctc accaactca caacaggctg 1380  
 gatgggtggg tggtaaaaag ggaaggatga ggctccccc atgtcacatt aaattcatgg 1440  
 ttttcattca aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 1532

&lt;210&gt; 56

&lt;211&gt; 410

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

Met	Glu	Leu	Pro	Ser	Gly	Pro	Gly	Pro	Glu	Arg	Leu	Phe	Asp	Ser	His
1															
														15	

Arg	Leu	Pro	Gly	Asp	Cys	Phe	Leu	Leu	Leu	Val	Leu	Leu	Tyr	Ala
													30	
20							25							

Pro	Val	Gly	Phe	Cys	Leu	Leu	Val	Leu	Arg	Leu	Phe	Leu	Gly	Ile	His
													45		
35							40								

Val	Phe	Leu	Val	Ser	Cys	Ala	Leu	Pro	Asp	Ser	Val	Leu	Arg	Arg	Phe
													60		
50							55								

Val	Val	Arg	Thr	Met	Cys	Ala	Val	Leu	Gly	Leu	Val	Ala	Arg	Gln	Glu
													80		
65							70								

Asp	Ser	Gly	Leu	Arg	Asp	His	Ser	Val	Arg	Val	Leu	Ile	Ser	Asn	His
													95		
85							90								

Val	Thr	Pro	Phe	Asp	His	Asn	Ile	Val	Asn	Leu	Leu	Thr	Thr	Cys	Ser
												110			
100							105								

Thr	Pro	Leu	Leu	Asn	Ser	Pro	Pro	Ser	Phe	Val	Cys	Trp	Ser	Arg	Gly
												125			
115							120								

Phe	Met	Glu	Met	Asn	Gly	Arg	Gly	Glu	Leu	Val	Glu	Ser	Leu	Lys	Arg
												140			
130							135								

Phe	Cys	Ala	Ser	Thr	Arg	Leu	Pro	Pro	Thr	Pro	Leu	Leu	Phe	Pro	
												160			
145							150								

Glu	Glu	Glu	Ala	Thr	Asn	Gly	Arg	Glu	Gly	Leu	Leu	Arg	Phe	Ser	Ser
												175			
165							170								

Trp	Pro	Phe	Ser	Ile	Gln	Asp	Val	Val	Gln	Pro	Leu	Thr	Leu	Gln	Val
												190			
180							185								

Gln Arg Pro Leu Val Ser Val Thr Val Ser Asp Ala Ser Trp Val Ser  
 195 200 205  
 Glu Leu Leu Trp Ser Leu Phe Val Pro Phe Thr Val Tyr Gln Val Arg  
 210 215 220  
 Trp Leu Arg Pro Val His Arg Gln Leu Gly Glu Ala Asn Glu Glu Phe  
 225 230 235 240  
 Ala Leu Arg Val Gln Gln Leu Val Ala Lys Glu Leu Gly Gln Thr Gly  
 245 250 255  
 Thr Arg Leu Thr Pro Ala Asp Lys Ala Glu His Met Lys Arg Gln Arg  
 260 265 270  
 His Pro Arg Leu Arg Pro Gln Ser Ala Gln Ser Ser Phe Pro Pro Ser  
 275 280 285  
 Pro Gly Pro Ser Pro Asp Val Gln Leu Ala Thr Leu Ala Gln Arg Val  
 290 295 300  
 Lys Glu Val Leu Pro His Val Pro Leu Gly Val Ile Gln Arg Asp Leu  
 305 310 315 320  
 Ala Lys Thr Gly Cys Val Asp Leu Thr Ile Thr Asn Leu Leu Glu Gly  
 325 330 335  
 Ala Val Ala Phe Met Pro Glu Asp Ile Thr Lys Gly Thr Gln Ser Leu  
 340 345 350  
 Pro Thr Ala Ser Ala Ser Lys Phe Pro Ser Ser Gly Pro Val Thr Pro  
 355 360 365  
 Gln Pro Thr Ala Leu Thr Phe Ala Lys Ser Ser Trp Ala Arg Gln Glu  
 370 375 380  
 Ser Leu Gln Glu Arg Lys Gln Ala Leu Tyr Glu Tyr Ala Arg Arg Arg  
 385 390 395 400  
 Phe Thr Glu Arg Arg Ala Gln Glu Ala Asp  
 405 410

<210> 57  
 <211> 2093  
 <212> DNA  
 <213> Homo sapiens

<400> 57  
 cgcgtttcag cgaagtcgca cgtgaaggat agcagtggcc tgagaaaagac ccagtcatgg 60  
 cagcctccag catcagttca ccatggggaa agcatgtgtt caaagccatt ctgatggtcc 120  
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 caggccaaaca gaagagagaa gccccagttt atgtcttgac ccagataggt cgatctgtgc 240  
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&lt;210&gt; 58

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 58

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Ala	Gln	Ser	Arg	Arg	Asp	Phe	Ala	Pro	Pro	Gly	Gln	Gln	Lys	Arg	Glu
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Ala	Pro	Val	Asp	Val	Leu	Thr	Gln	Ile	Gly	Arg	Ser	Val	Arg	Gly	Thr
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Leu	Asp	Ala	Trp	Ile	Gly	Pro	Glu	Thr	Met	His	Leu	Val	Ser	Glu	Ser
			65					70							80

Ser	Ser	Gln	Val	Leu	Trp	Ala	Ile	Ser	Ser	Ala	Ile	Ser	Val	Ala	Phe
															85
															90

Phe	Ala	Leu	Ser	Gly	Ile	Ala	Ala	Gln	Leu	Leu	Asn	Ala	Leu	Gly	Leu
															100
															105

Ala	Gly	Asp	Tyr	Leu	Ala	Gln	Gly	Leu	Lys	Leu	Ser	Pro	Gly	Gln	Val
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Gln	Thr	Phe	Leu	Leu	Trp	Gly	Ala	Gly	Ala	Leu	Val	Val	Tyr	Trp	Leu
			130					135							140

Leu	Ser	Leu	Leu	Leu	Gly	Leu	Val	Leu	Ala	Leu	Leu	Gly	Arg	Ile	Leu
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															150
															155

160

Trp Gly Leu Lys Leu Val Ile Phe Leu Ala Gly Phe Val Ala Leu Met  
 165 170 175

Arg Ser Val Pro Asp Pro Ser Thr Arg Ala Leu Leu Leu Ala Leu  
 180 185 190

Leu Ile Leu Tyr Ala Leu Leu Ser Arg Leu Thr Gly Ser Arg Ala Ser  
 195 200 205

Gly Ala Gln Leu Glu Ala Lys Val Arg Gly Leu Glu Arg Gln Val Glu  
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Glu Glu Glu

<210> 59

<211> 1372

<212> DNA

<213> Homo sapiens

<400> 59

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<210> 60

<211> 313

<212> PRT

<213> Homo sapiens

<400> 60

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35	40	45
Ala Tyr Lys Phe His Met Gly Leu Tyr Gly Glu Thr Gly Arg Leu Phe		
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Thr Glu Ser Cys Ser Ile Ser Pro Lys Leu Arg Ser Ile Ala Val Tyr		
65	70	75
Tyr Asp Asn Pro His Met Val Pro Pro Asp Lys Cys Arg Cys Ala Val		
85	90	95
Gly Ser Ile Leu Ser Glu Gly Glu Ser Pro Ser Pro Glu Leu Ile		
100	105	110
Asp Leu Tyr Gln Lys Phe Gly Phe Lys Val Phe Ser Phe Pro Ala Pro		
115	120	125
Ser His Val Val Thr Ala Thr Phe Pro Tyr Thr Thr Ile Leu Ser Ile		
130	135	140
Trp Leu Ala Thr Arg Arg Val His Pro Ala Leu Asp Thr Tyr Ile Lys		
145	150	155
160		
Glu Arg Lys Leu Cys Ala Tyr Pro Arg Leu Glu Ile Tyr Gln Glu Asp		
165	170	175
Gln Ile His Phe Met Cys Pro Leu Ala Arg Gln Gly Asp Phe Tyr Val		
180	185	190
Pro Glu Met Lys Glu Thr Glu Trp Lys Trp Arg Gly Leu Val Glu Ala		
195	200	205
Ile Asp Thr Gln Val Asp Gly Thr Gly Ala Asp Thr Met Ser Asp Thr		
210	215	220
Ser Ser Val Ser Leu Glu Val Ser Pro Gly Ser Arg Glu Thr Ser Ala		
225	230	235
240		
Ala Thr Leu Ser Pro Gly Ala Ser Ser Arg Gly Trp Asp Asp Gly Asp		
245	250	255
Thr Arg Ser Glu His Ser Tyr Ser Glu Ser Gly Ala Ser Gly Ser Ser		
260	265	270
Phe Glu Glu Leu Asp Leu Glu Gly Glu Gly Pro Leu Gly Glu Ser Arg		
275	280	285
Leu Asp Pro Gly Thr Glu Pro Leu Gly Thr Thr Lys Trp Leu Trp Glu		
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Pro Thr Ala Pro Glu Lys Gly Lys Glu		
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<210> 61  
 <211> 1529  
 <212> DNA

<213> Homo sapiens

<400> 61

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<210> 62

<211> 136

<212> PRT

<213> Homo sapiens

<400> 62

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Gln Gly Gln Gln Met Leu Ala Gly Gln Leu Leu Pro Met Leu Thr Leu  
35 40 45

Leu Pro Pro Ser Phe Pro Leu Pro His Pro Thr Leu Gly Pro Arg Arg  
50 55 60

His Ala Ser Leu Thr Gln Leu Gly Pro Ala Phe Trp Met Ala Trp Gly  
65 70 75 80

Arg Pro Trp Ala His Leu Gly Pro Gly Gln Pro Leu Gly Gln Leu Trp  
85 90 95

Lys Ser Ser Val Glu Glu His Leu Leu Ala Ala Trp Leu Gln Pro Leu  
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Ala Leu Leu Glu Trp Ser Leu Gly Ala Ser Ala Leu Ser Ala Leu Gly  
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Thr Ser His Pro Leu Gly Leu Gln  
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<210> 63  
<211> 2242  
<212> DNA  
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<210> 64  
<211> 447  
<212> PRT  
<213> Homo sapiens

<400> 64  
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Arg Ala Gly Glu Glu Arg Ser Gly Arg Pro Ala Cys Gln Lys Ala Asn  
 35 40 45  
 Gly Phe Pro Pro Asp Lys Ser Ser Gly Ser Lys Lys Gln Lys Gln Tyr  
 50 55 60  
 Gln Arg Ile Arg Lys Glu Lys Pro Gln Gln His Asn Phe Thr His Arg  
 65 70 75 80  
 Leu Leu Ala Ala Ala Leu Lys Ser His Ser Gly Asn Ile Ser Cys Met  
 85 90 95  
 Asp Phe Ser Ser Asn Gly Lys Tyr Leu Ala Thr Cys Ala Asp Asp Arg  
 100 105 110  
 Thr Ile Arg Ile Trp Ser Thr Lys Asp Phe Leu Gln Arg Glu His Arg  
 115 120 125  
 Ser Met Arg Ala Asn Val Glu Leu Asp His Ala Thr Leu Val Arg Phe  
 130 135 140  
 Ser Pro Asp Cys Arg Ala Phe Ile Val Trp Leu Ala Asn Gly Asp Thr  
 145 150 155 160  
 Leu Arg Val Phe Lys Met Thr Lys Arg Glu Asp Gly Gly Tyr Thr Phe  
 165 170 175  
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 180 185 190  
 Asp Ile Gly Ile Ala Asn Thr Gly Lys Phe Ile Met Thr Ala Ser Ser  
 195 200 205  
 Asp Thr Thr Val Leu Ile Trp Ser Leu Lys Gly Gln Val Leu Ser Thr  
 210 215 220  
 Ile Asn Thr Asn Gln Met Asn Asn Thr His Ala Ala Val Ser Pro Cys  
 225 230 235 240  
 Gly Arg Phe Val Ala Ser Cys Gly Phe Thr Pro Asp Val Lys Val Trp  
 245 250 255  
 Glu Val Cys Phe Gly Lys Lys Gly Glu Phe Gln Glu Val Val Arg Ala  
 260 265 270  
 Phe Glu Leu Lys Gly His Ser Ala Ala Val His Ser Phe Ala Phe Ser  
 275 280 285  
 Asn Asp Ser Arg Arg Met Ala Ser Val Ser Lys Asp Gly Thr Trp Lys  
 290 295 300  
 Leu Trp Asp Thr Asp Val Glu Tyr Lys Lys Gln Asp Pro Tyr Leu  
 305 310 315 320  
 Leu Lys Thr Gly Arg Phe Glu Glu Ala Ala Gly Ala Ala Pro Cys Arg  
 325 330 335  
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 340 345 350

Ser Ile His Leu Tyr Asn Thr Arg Arg Gly Glu Lys Glu Glu Cys Phe  
355 360 365  
Glu Arg Val His Gly Glu Cys Ile Ala Asn Leu Ser Phe Asp Ile Thr  
370 375 380  
Gly Arg Phe Leu Ala Ser Cys Gly Asp Arg Ala Val Arg Leu Phe His  
385 390 395 400  
Asn Thr Pro Gly His Arg Ala Met Val Glu Glu Met Gln Gly His Leu  
405 410 415  
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420 425 430  
Thr Gln Ala Gln Glu Thr Leu Lys Ser Leu Gly Ala Leu Lys Lys  
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<400> 73  
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<210> 77  
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21

20

19

20

19

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<220>  
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 Ile Thr Ser Gln Thr Asn Lys Lys Gln Thr Arg Glu Thr Cys Tyr Ala  
 35 40 45  
 His Ser Ala Glu Glu Ile Gly Ile Ile Ala Gly Lys Arg Ile His Arg  
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 35 40 45  
 Ala Asn Ser Leu Cys Glu Pro Arg Thr Pro Asp Pro Lys Pro Ile Asn  
 50 55 60  
 Gly Lys Gly Asp Met Gly Val Pro Ser Gln Glu Thr Pro Val Pro Phe  
 65 70 75 80  
 Leu Ser Cys Leu Phe Pro Leu Thr Ser Leu Trp Phe Phe Ile Phe Lys  
 85 90 95

Cys Phe Asn Phe Cys Ile Phe Phe Ser Leu Arg Glu Tyr Leu Leu Ile  
 100 105 110

Ser Asp Val Gln Gly Val Ala Thr Glu Lys Pro Leu Ser Ser Ser Val  
 115 120 125

Cys Arg Gly Val Trp Pro Cys Gly Leu Gly Gly Ala Val Ile Leu Pro  
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<210> 99

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<212> PRT

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<400> 99

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 20 25 30

Ser Cys Ser Leu Thr Trp Glu Thr Pro Arg Trp Tyr Met Ala Gly Arg  
 35 40 45

Val Ala Thr Ser Thr Ser Gly Cys His Cys Trp Met Ser Arg Arg Asp  
 50 55 60

Leu Thr Pro Leu Pro His Pro Ser Glu Pro Gly Val Leu Asp Cys Leu  
 65 70 75 80

Gly Pro Cys His Leu Leu Pro Leu Leu Ser Pro Gly Ser Pro Cys Trp  
 85 90 95

Val Leu Gly Leu His Phe Ser Leu His Pro Pro Ser Ala Ala Ser Ala  
 100 105 110

Ser His Ala Leu Thr Ile Thr Ser Leu Pro Pro Gly Leu Leu Pro Phe  
 115 120 125

Val Gly Val Glu Leu Thr Ala His Pro Gln Ala Leu Met Gly Arg Gly  
 130 135 140

Phe Pro Ser Gly Met Ala Ala Ala Gly Arg His Leu Cys Phe Leu  
 145 150 155

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<211> 54

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<400> 100

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His Leu Phe Phe His Ile Asn Phe Lys Leu Cys Pro Val Leu His Pro  
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Leu Ser His Ser His Pro Gln Ile Leu Gly Ser Val Ile Pro Cys Ala  
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Ile Ile Phe Pro Pro Leu  
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<210> 101  
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His Ser Met Asn Gly Arg Cys Thr Asp His Phe Leu Phe Val Leu Ser  
 20 25 30

Ser Leu Leu Ser Pro Ala Ala Ile Leu Val Arg Leu Val Pro Ala Arg  
 35 40 45

Glu Arg Cys Pro Gln Val Lys Gly Tyr Ser Gly Thr Trp Glu Lys Ala  
 50 55 60

Pro Gly Arg Phe Pro Cys Gly Pro Ala Gln His Gly Ser Arg Val Gly  
 65 70 75 80

Thr Leu Leu Cys Arg Gln Pro Ser Leu Tyr Ser Ser Gly Phe Leu Arg  
 85 90 95

Ala Leu Pro Cys Leu Cys Gln Ala Cys Ala Ala Ser His Pro Thr Ala  
 100 105 110

Ala Trp Glu Arg Pro Ala Thr Leu Pro Val His Thr Leu Pro Val His  
 115 120 125

Thr Leu Pro Val His Asn Cys Ser Arg Ala Leu Cys Leu Trp Ala Pro  
 130 135 140

Asn Pro Ser Ser Cys Ser Thr Phe Val Trp His Gly Asp Leu Cys Phe  
 145 150 155 160

Phe Ser Trp Cys Leu Cys Val Trp Ala Trp Asp Glu Cys Trp Tyr Ala  
 165 170 175

Leu Arg Thr Phe Leu Ile Ala Pro Cys Thr Leu Glu His Gly Ala Asp  
 180 185 190

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 195 200 205

Thr Leu Glu Arg  
 210

&lt;210&gt; 102

&lt;211&gt; 73

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

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1															

Arg	Ser	Pro	Glu	Asp	Ser	Val	Glu	Gly	Ser	Val	Asp	Ser	Lys	Ser	Gly
							20						30		

Phe	Ser	Ser	Ile	Ala	Lys	Lys	Arg	Ser	Ala	Ala	Glu	Thr	Thr	Ser	Gly
							35					45			

Tyr	Pro	Arg	Pro	Pro	Ala	Phe	Glu	Leu	Gly	Asp	Leu	Pro	Cys	Leu	Ile
							50				55		60		

Leu	Ser	His	Thr	Cys	Phe	Phe	Thr	Arg
							65	

70

&lt;210&gt; 103

&lt;211&gt; 302

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

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1															

Leu	Phe	Pro	Gly	Ala	Trp	Ala	Gln	Gly	His	Val	Pro	Pro	Gly	Cys	Ser
							20				25		30		

Gln	Gly	Leu	Asn	Pro	Leu	Tyr	Tyr	Asn	Leu	Cys	Asp	Arg	Ser	Gly	Ala
							35				40		45		

Trp	Gly	Ile	Val	Leu	Glu	Ala	Val	Ala	Gly	Ala	Gly	Ile	Val	Thr	Thr
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Phe	Val	Leu	Thr	Ile	Ile	Leu	Val	Ala	Ser	Leu	Pro	Phe	Val	Gln	Asp
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Thr	Lys	Lys	Arg	Ser	Leu	Leu	Gly	Thr	Gln	Val	Phe	Phe	Leu	Leu	Gly
							85				90		95		

Thr	Leu	Gly	Leu	Phe	Cys	Leu	Val	Phe	Ala	Cys	Val	Val	Lys	Pro	Asp
							100				105		110		

Phe	Ser	Thr	Cys	Ala	Ser	Arg	Arg	Phe	Leu	Phe	Gly	Val	Leu	Phe	Ala
							115				120		125		

Ile	Cys	Phe	Ser	Cys	Leu	Ala	Ala	His	Val	Phe	Ala	Leu	Asn	Phe	Leu
							130				135		140		

Ala	Arg	Lys	Asn	His	Gly	Pro	Arg	Gly	Trp	Val	Ile	Phe	Thr	Val	Ala
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Leu Leu Leu Thr Leu Val Glu Val Ile Ile Asn Thr Glu Trp Leu Ile  
 165 170 175  
 Ile Thr Leu Val Arg Gly Ser Gly Glu Gly Pro Gln Gly Asn Ser  
 180 185 190  
 Ser Ala Ala Gly Pro Trp Pro Pro Pro Val Pro Ser Pro Thr Trp Thr  
 195 200 205  
 Leu Ser Trp His Ser Ser Thr Ser Cys Cys Cys Cys Trp Val Pro Ser  
 210 215 220  
 Trp Gly Pro Gly Pro Pro Cys Val Ala Ala Thr Ser Ala Gly Val Ser  
 225 230 235 240  
 Met Gly Ser Leu Cys Ser Ser Pro Gln Pro Pro Pro Leu Pro Tyr Gly  
 245 250 255  
 Trp Cys Gly Ser Ser Cys Ile Leu Thr Ala Thr Ser Ser Thr Thr Val  
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 Arg Ala Cys Pro Thr Ser Glu Val Leu Gly Phe Arg Val Leu Cys Leu  
 35 40 45  
 Pro Leu Pro Val Pro Arg Ser Ser Gln Thr Leu Leu Leu Phe Ile Arg  
 50 55 60  
 Ala Val Gly Arg Val Phe Leu Leu Phe Leu Gly Thr Cys Pro Cys Ser  
 65 70 75 80  
 Ser His Cys Pro Pro Cys Leu Ser Leu Ile Gln Met Cys His His Gly  
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<210> 105

<211> 18  
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Gly Val

<210> 106  
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 <213> Homo sapiens

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 20 25 30

Thr Asn Ile Gly Glu Ala Leu Gly His Gly Leu Gly Asp Ala Leu Ser  
 35 40 45

Glu Gly Val Gly Lys Ala Ile Gly Lys Glu Ala Gly Gly Ala Ala Gly  
 50 55 60

Ser Lys Val Ser Glu Ala Leu Gly Gln Gly Thr Arg Glu Ala Val Gly  
 65 70 75 80

Thr Gly Val Arg Gln Val Pro Gly Phe Gly Val Ala Asp Ala Leu Gly  
 85 90 95

Asn Arg Val Gly Glu Ala Ala His Ala Leu Gly Asn Thr Gly His Glu  
 100 105 110

Ile Gly Arg Gln Ala Glu Asp Val Ile Arg His Gly Ala Asp Ala Val  
 115 120 125

Arg Gly Ser Trp Gln Gly Val Pro Gly His Asn Gly Ala Trp Glu Thr  
 130 135 140

Ser Gly Gly His Gly Ile Phe Gly Ser Gln Gly Gly Leu Gly Gly Gln  
 145 150 155 160

Gly Gln Gly Asn Pro Gly Gly Leu Gly Thr Pro Trp Val His Gly Tyr  
 165 170 175

Pro Gly Asn Ser Ala Gly Ser Phe Gly Met Asn Pro Gln Gly Ala Pro  
 180 185 190

Trp Gly Gln Gly Gly Asn Gly Gly Pro Pro Asn Phe Gly Thr Asn Thr  
 195 200 205

Gln Gly Ala Val Ala Gln Pro Gly Tyr Gly Ser Val Arg Ala Ser Asn  
 210 215 220

Gln Asn Glu Gly Cys Thr Asn Pro Pro Pro Ser Gly Ser Gly Gly Gly  
 225 230 235 240  
 Ser Ser Asn Ser Gly Gly Ser Gly Ser Gln Ser Gly Ser Ser Gly  
 245 250 255  
 Ser Gly Ser Asn Gly Asp Asn Asn Asn Gly Ser Ser Ser Gly Gly Ser  
 260 265 270  
 Ser Ser Gly Ser Ser Ser Gly Gly Ser Ser Gly Gly Ser Ser Gly Gly  
 275 280 285  
 Ser Ser Gly Asn Ser Gly Gly Ser Arg Gly Asp Ser Gly Ser Glu Ser  
 290 295 300  
 Ser Trp Gly Ser Ser Thr Gly Ser Ser Ser Gly Asn His Gly Gly Ser  
 305 310 315 320  
 Gly Gly Gly Asn Gly His Lys Pro Gly Asn Ser Glu Thr Ser Pro Gly  
 325 330 335  
 Met Phe Asn Phe Asp Thr Phe Trp Lys Asn Phe Lys Ser Lys Leu Gly  
 340 345 350  
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&lt;210&gt; 107

&lt;211&gt; 74

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

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 1 5 10 15

Gln Cys Gly Gly Ala Leu Ala Cys Ser Leu Ala Ser Ala Ser Gly Thr  
 20 25 30

Ala Gly Val Val Pro Gly Ser Phe Cys Thr Val Gly Phe Gly Asp Val  
 35 40 45

Ser Pro Thr Trp Val Thr Val Gly Leu Pro His Pro Glu Arg Ser Val  
 50 55 60

Ser Thr Pro Glu Thr Leu Ser Val Ser Pro  
 65 70

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/08504

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07H 21/04; C07K 14/435; C12N 1/20; C12P 21/02; A61K 38/00  
 US CL : 536/23.5; 530/351; 435/252.3, 69.5; 514/2

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5; 530/351; 435/252.3, 69.5; 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database Medline on STN, pir60: Accession No:C434597; reference No:A35796. GERSHON, P. D. and MOSS, B. Early transcription factor subunits are encoded by vaccinia virus late genes. Proc. Natl. Acad. Sci. U.S.A. 1990, Vol. 87, pages 4401-4405. Amino Acids LQVGKGQEV.	9
X	Database Medline on STN, swiss-prot37. Accession No:P49682. LOETSCHER et al. Chemokine receptor specific for IP10 and mig: structure, function, and expression in activated T-lymphocytes. 1996. J. EXP. MED. Vol. 184, pages 963-969. Amino acids: ALYSLLFL.	9

 Further documents are listed in the continuation of Box C. See patent family annex.

• Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search  
08 JULY 1999

Date of mailing of the international search report

30 AUG 1999

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231  
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EILEEN F. O'HARA  
Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/08504

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on STN, EST: Accession No:T35343. ADAMS et al. EST83120 Homo sapiens cDNA 5' end similar to None. Initial assesment of human gene diversity and expression patterns based upon 52 million basepairs of cDNA sequence. Available in database Sept. 6, 1995. 100% sequence match over 297 nucleotide bases, corresponding to nucleotides 156 to 453 of SEQ ID NO:1.	1-11

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US99/08504

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US99/08504

**B. FIELDS SEARCHED**

Electronic data bases consulted (Name of data base and where practicable terms used):

SEQUENCE DATA BASE MPSRCH: GenEmbl, EST, N\_Geneseq\_34, Issued\_Patents\_NA, PIR\_58, SwissProt\_36, STREMBL\_8, A\_Geneseq\_34, Issued\_Patents\_AA, pir60, SwissProt\_37,pir\_60, sptremb19, a-geneseq35, a-issued

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-11, drawn to polynucleotides comprising SEQ ID NO:1, the protein encoded by that polynucleotide comprising SEQ ID NO:2, host cells containing said polynucleotides, a recombinant process for producing protein, and a pharmaceutical composition comprising the protein.

Group II, claims 12 and 13, drawn to a polynucleotide comprising SEQ ID NO: 3 and a protein comprising SEQ ID NO: 4.

Group III, claims 14 and 15, drawn to a polynucleotide comprising SEQ ID NO: 5 and a protein comprising SEQ ID NO: 6.

Group IV, claims 16 and 17, drawn to a polynucleotide comprising SEQ ID NO: 7 and a protein comprising SEQ ID NO.

Group V, claims 18 and 19, drawn to a polynucleotide comprising SEQ ID NO: 9 and a protein comprising SEQ ID NO: 10.

Group VI, claims 20 and 21, drawn to a polynucleotide comprising SEQ ID NO: 11 and a protein comprising SEQ ID NO: 12.

Group VII, claims 22 and 23, drawn to a polynucleotide comprising SEQ ID NO: 13 and a protein comprising SEQ ID NO: 14.

Group VIII, claims 24 and 25, drawn to a polynucleotide comprising SEQ ID NO: 15 and a protein comprising SEQ ID NO: 16.

Group IX, claims 26 and 27, drawn to a polynucleotide comprising SEQ ID NO: 17 and a protein comprising SEQ ID NO: 18.

Group X, claims 28 and 29, drawn to a polynucleotide comprising SEQ ID NO: 19 and a protein comprising SEQ ID NO: 20.

Group XI, claims 30 and 31, drawn to a polynucleotide comprising SEQ ID NO: 21 and a protein comprising SEQ ID NO: 22.

Group XII, claims 32 and 33, drawn to a polynucleotide comprising SEQ ID NO: 23 and a protein comprising SEQ ID NO: 24.

Group XIII, claims 34 and 35, drawn to a polynucleotide comprising SEQ ID NO: 25 and a protein comprising SEQ ID NO: 26.

Group XIV, claims 36 and 37, drawn to a polynucleotide comprising SEQ ID NO: 27 and a protein comprising SEQ ID NO: 28.

Group XV, claims 38 and 39, drawn to a polynucleotide comprising SEQ ID NO: 29 and a protein comprising SEQ ID NO: 30.

Group XVI, claims 40 and 41, drawn to a polynucleotide comprising SEQ ID NO: 31 and a protein comprising SEQ ID NO: 32.

Group XVII, claims 42 and 43, drawn to a polynucleotide comprising SEQ ID NO: 33 and a protein comprising SEQ ID NO: 34.

Group XVIII, claims 44 and 45, drawn to a polynucleotide comprising SEQ ID NO: 35 and a protein comprising SEQ ID NO: 36.

Group XIX, claims 46 and 47, drawn to a polynucleotide comprising SEQ ID NO: 37 and a protein comprising SEQ ID NO: 38.

Group XX, claims 48 and 49, drawn to a polynucleotide comprising SEQ ID NO: 39 and a protein comprising SEQ ID NO: 40.

Group XXI, claims 50 and 51, drawn to a polynucleotide comprising SEQ ID NO: 41 and a protein comprising SEQ ID NO: 42.

Group XXII, claims 52 and 53, drawn to a polynucleotide comprising SEQ ID NO: 43 and a protein comprising SEQ ID NO: 44.

Group XXIII, claims 54 and 55, drawn to a polynucleotide comprising SEQ ID NO: 45 and a protein comprising SEQ ID NO: 46.

Group XXIV, claims 56 and 57, drawn to a polynucleotide comprising SEQ ID NO: 47 and a protein comprising SEQ

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US99/08504

ID NO: 48.

Group XXV, claims 58 and 59, drawn to a polynucleotide comprising SEQ ID NO: 49 and a protein comprising SEQ ID NO: 50.

Group XXVI, claims 60 and 61, drawn to a polynucleotide comprising SEQ ID NO: 51 and a protein comprising SEQ ID NO: 52.

Group XXVII, claims 62 and 63, drawn to a polynucleotide comprising SEQ ID NO: 53 and a protein comprising SEQ ID NO: 54.

Group XXVIII, claims 64 and 65, drawn to a polynucleotide comprising SEQ ID NO: 55 and a protein comprising SEQ ID NO: 56.

Group XXIX, claims 66 and 67, drawn to a polynucleotide comprising SEQ ID NO: 57 and a protein comprising SEQ ID NO: 58.

Group XXX, claims 68 and 69, drawn to a polynucleotide comprising SEQ ID NO: 59 and a protein comprising SEQ ID NO: 60.

Group XXXI, claims 70 and 71, drawn to a polynucleotide comprising SEQ ID NO: 61 and a protein comprising SEQ ID NO: 62.

Group XXXII, claims 72 and 73, drawn to a polynucleotide comprising SEQ ID NO: 63 and a protein comprising SEQ ID NO: 64.

The inventions listed as Groups I-XXXII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Pursuant to 37 C.F.R. § 1.475 (b-d), the ISA/US considers that where multiple processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first recited product, a polynucleotide comprising SEQ ID NO:1, the polypeptide it encodes comprising SEQ ID NO:2, vectors comprising the polynucleotides, host cells containing the polynucleotides and methods of producing the polypeptide.

Further pursuant to 37 C.F.R. § 1.475(b-d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.